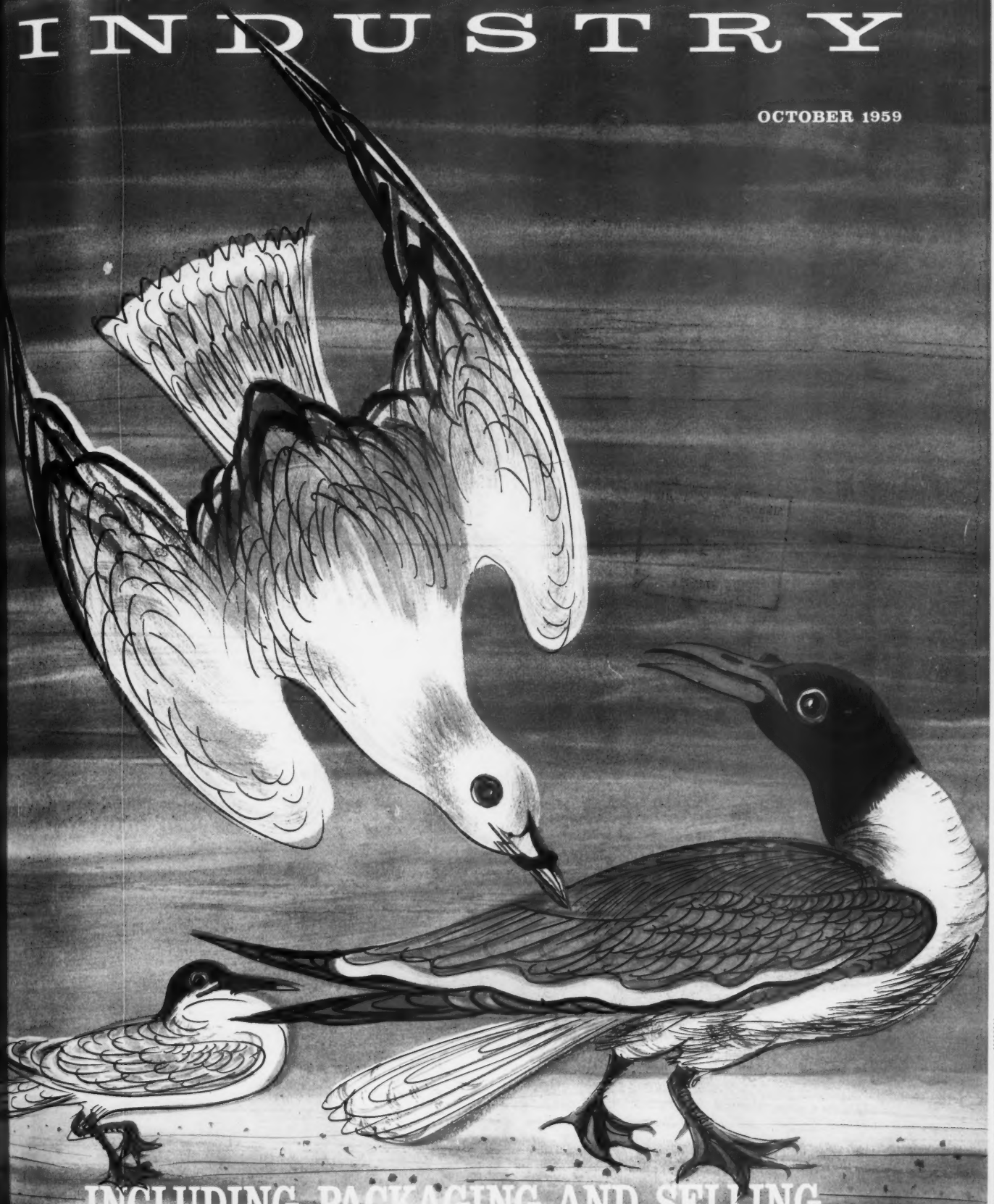
DRUG & COSMETIC INDUSTRY

OCTOBER 1959



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Drug and Cosmetic Industry

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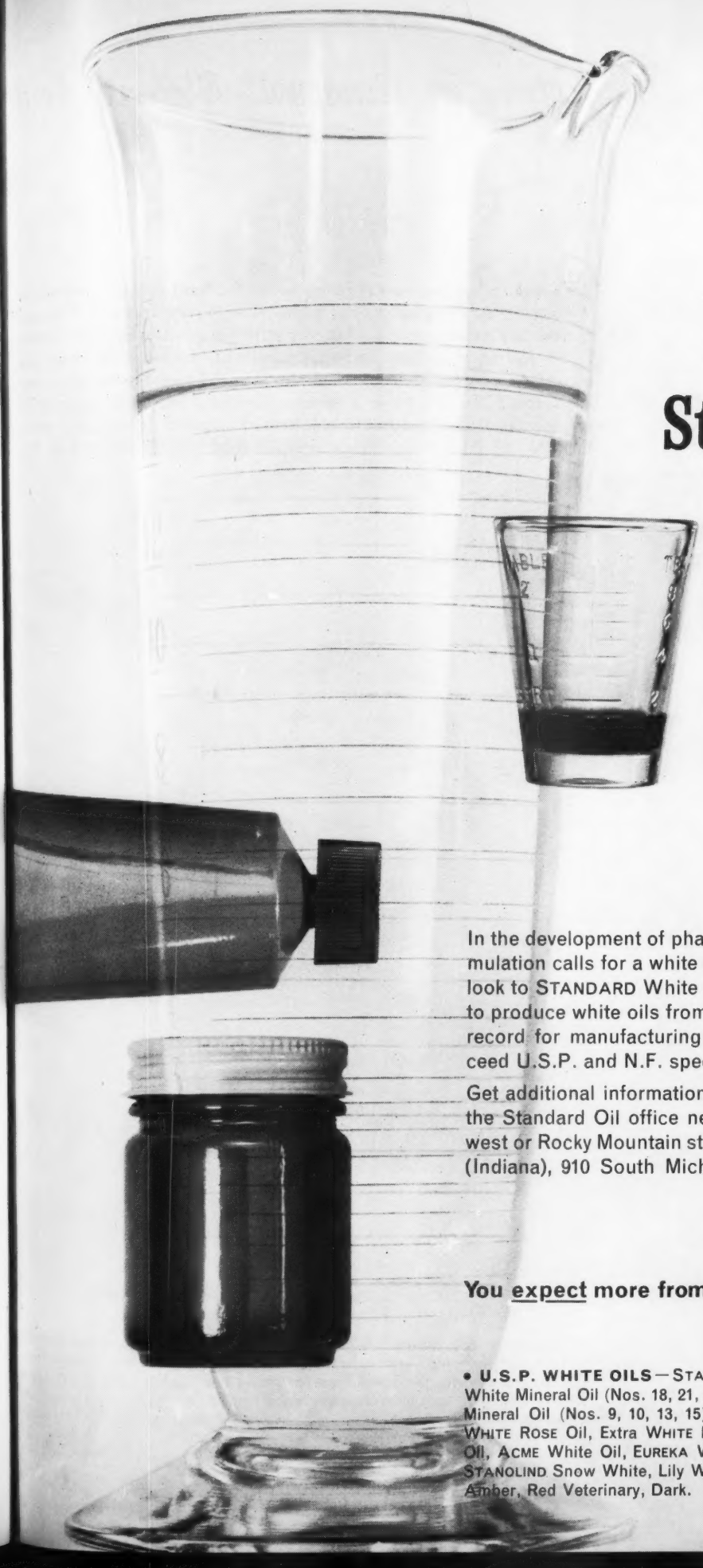

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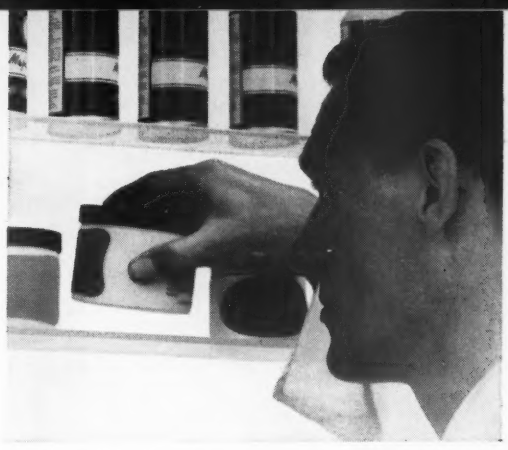
Women instinctively sense cosmetic quality from the color of the product. She likes white to be *really* white and pastel colors to be true and pure. Premium cosmetic manufacturers have proved she'll even pay a few cents more to get this extra luxury. So, to keep milady sold and protect their valuable brand names, many major cosmetic and toiletry producers use only Emersol 132, the *whitest* triple-pressed stearic acid available.

keep customers coming back for more



First class toiletries and cosmetics face a shelf life problem unless they contain a stearic acid with excellent *oxidation stability*. Emersol 132 Lily provides this important characteristic even throughout long storage periods. This means more protection against deterioration resulting from changes in color, clarity, emulsion stability, texture and consistency.

Pure? You bet! Drug companies use only the very *purest*, the very finest stearic acid in their pharmaceuticals. And, that's why many of them specify Emersol 132 (which exceeds U.S.P. standards) and will accept no substitutions.

For table charm, a trim, sturdy candle—straight as a light beam and whiter than the cloth it graces. Once again Emersol pressed-type stearic acids, with an unvarying crystalline structure, get the credit. These crystalline stearic acids form a strong, unyielding candle. And, by shrinking just the right amount, they separate cleanly from the mold and eliminate breakage.

Making clothes soft and WHITE poses special problems. The strong acids and intense heat used in manufacturing tend to discolor textile softeners derived from stearic acid. So, quality conscious softener producers look for a high degree of *color stability* in the stearic acid they order—and Emersol Stearic Acids usually get the nod. Color stability is one of their most outstanding characteristics.

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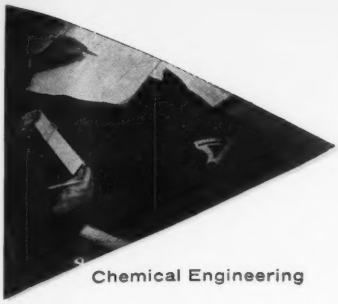
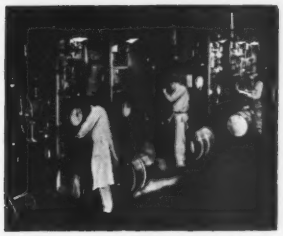


Chemical Engineering

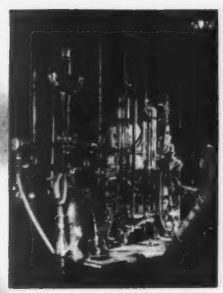
Quality Control



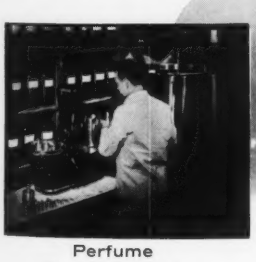
Chemical Manufacturing

Perfume
Evaluation Board

Sales



Aromatic
Chemical Research



Perfume
Oil Production

Creative Perfumer

Cosmetic Research

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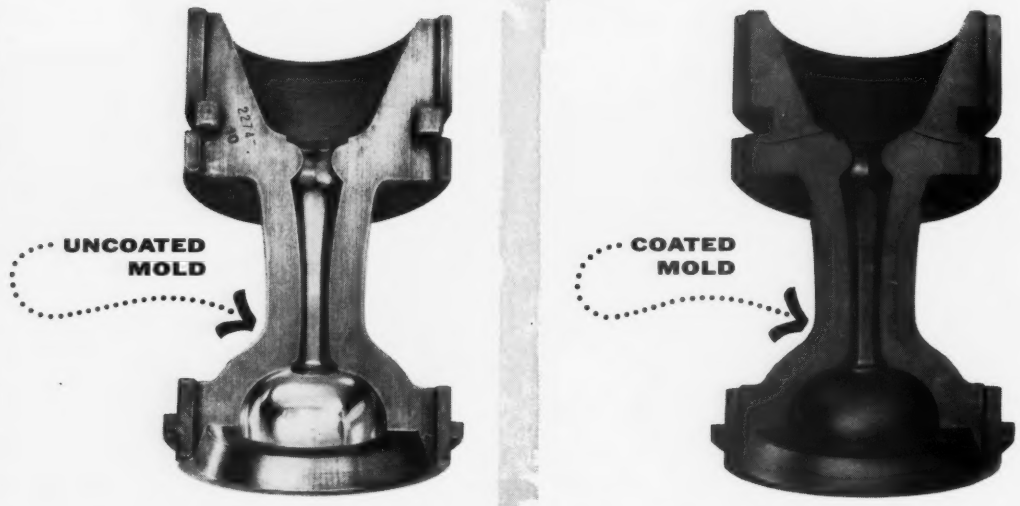
B.F.Goodrich Chemical *raw materials*



Glas-Mel *is manufactured by Delos M. Palmer & Associates, Toledo, Ohio, using Carbopol 934. This mold release eliminates fumes and fire hazard, and increases glass production rates by preventing wetting of glass to molds, reducing defects, and reducing mold maintenance. B.F.Goodrich Chemical Company supplies the Carbopol water-soluble resin.*

New water-based lubricant and mold release agent made possible by Carbopol

A new spray lubricant for lining glassware molds is being made with Carbopol 934 as a dispersing and suspending agent. This new mold release is water-based, replacing the oils, greases and organic materials previously used. It provides a superior, thin, tenacious film and at the same time eliminates a cause of fumes and fire hazard.

Carbopol 934 provides ideal colloidal suspension, permitting variation in desired viscosity by varying the concentration. For example, 0.5% Carbopol 934 produces stable suspensions with high viscosities, 0.3% provides stable suspensions with very low viscosity. It proved ideal for this colloidal suspension of microsized molybdenum disulfide. And the suspension is permanent—there is no need for a "shake well before using" on the container.

Carbopol water-soluble resins may be the answer to your need for an improved product, or a broader market. Information and samples can be obtained by writing Dept. DB-5, B.F.Goodrich Chemical Company, 3135 Euclid Avenue, Cleveland 15, Ohio. Cable address: Goodchemco. In Canada: Kitchener, Ontario.

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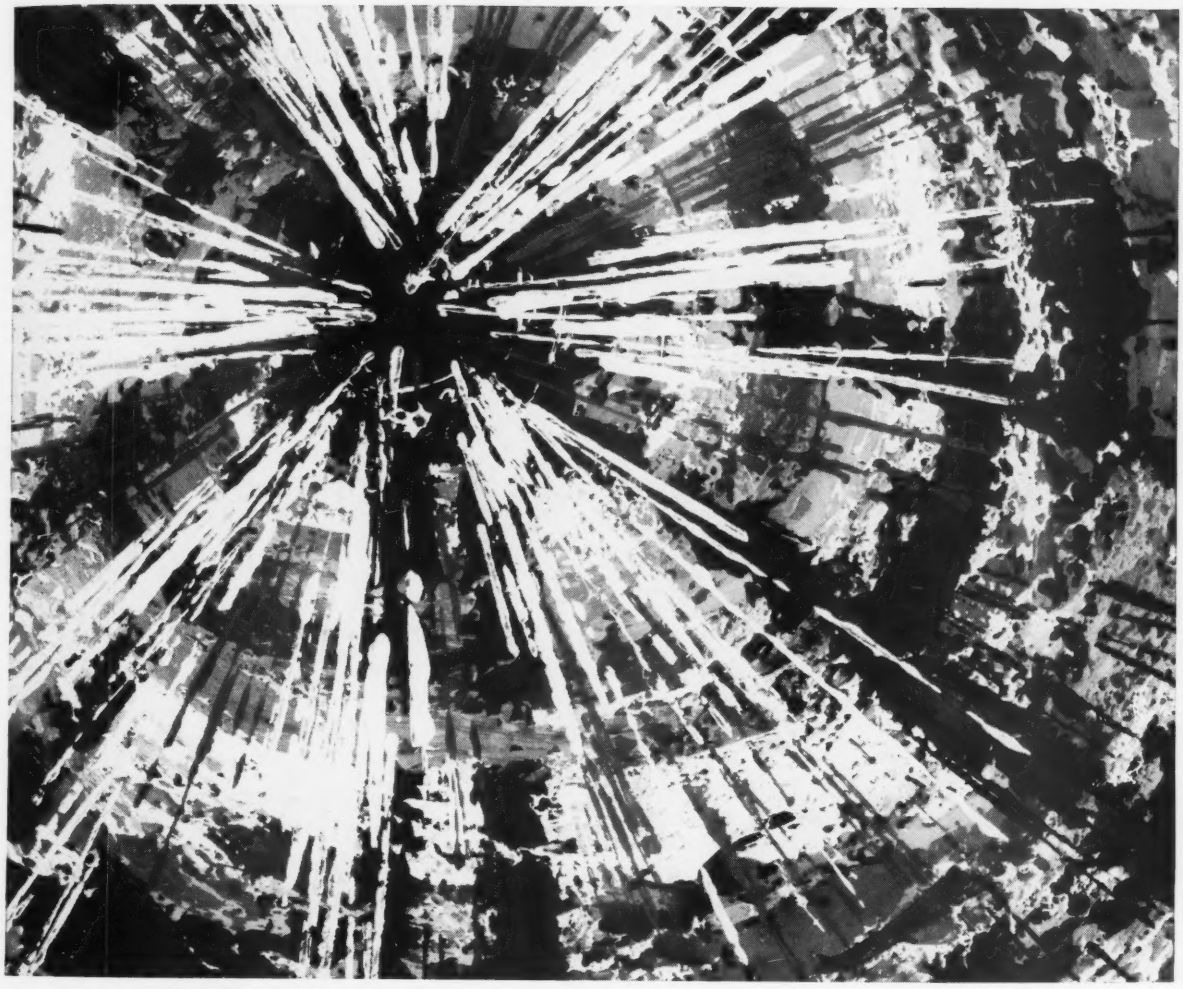

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RESEDALIA—Is an Acetal. Its merit has been well proven in actual use. As its name implies, its aroma is reminiscent of Reseda Mignonette. As a blending agent it has an harmonizing effect wherever it is employed.

FLORANOL—Is an Ester with an Apricot-Rose note. It blends well with all types of Rose ingredients.

Sole representative in the United States for
J. & E. Sozio, Grasse, France.

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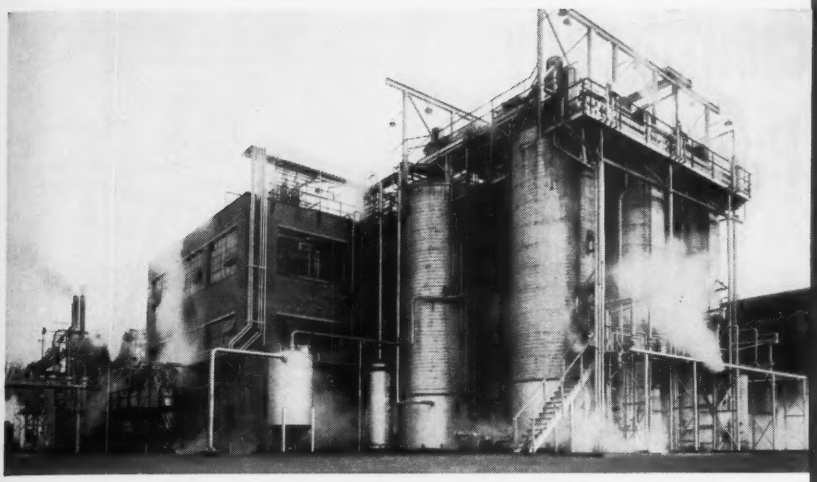
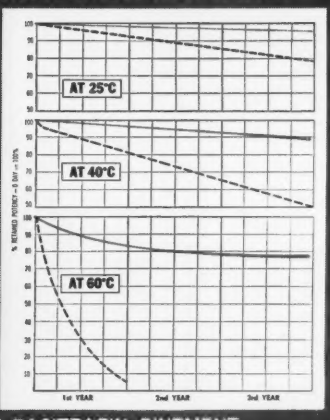


Typical Curves Showing Thermal Stability of

ZINC BACITRACIN
(red solid line)
VS.
REGULAR BACITRACIN
(black broken line)

● NON-FORMULATED POWDER



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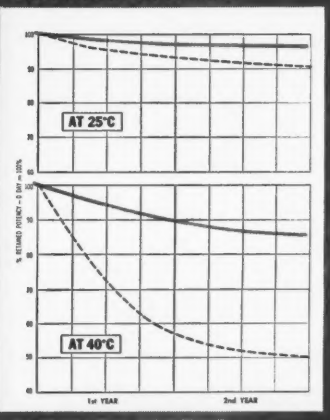
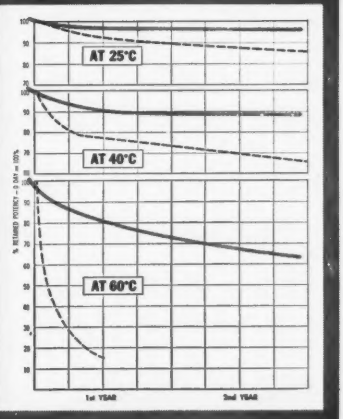


● BACITRACIN TROCHES



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when formulating preparations containing bacitracin.

The use of bacitracin in pharmaceutical compounds is growing rapidly because this antibiotic has proved non-allergenic, non-absorptive, and non-irritating. Commercial Solvents Corporation manufactures and sells both regular and zinc bacitracin, but, for topical applications zinc bacitracin is the better buy.

STABLE: Zinc bacitracin offers superior activity stability at room and elevated temperatures. Stability is maintained even at the high temperatures required in the manufacture of pharmaceuticals needing heated ointment or suppository bases, oven-drying of granulations, molten sugars for candy troches.

ECONOMICAL: Zinc bacitracin stored for two years at 40° still passed the FDA minimum potency requirements. Storage and thermal stability eliminate the need for utilizing a high percentage of excess antibiotic, and reduce product cost.

SYNERGISTIC: Zinc bacitracin is currently being combined with other antibiotics such as neomycin. Tablet and ointment formulations of zinc bacitracin and neomycin are stable, economical and provide broad-spectrum coverage.

LESS BITTER: Zinc bacitracin is inherently less bitter tasting than bacitracin. In addition, the taste of zinc bacitracin is much more easily masked than that of bacitracin.

Commercial Solvents Corporation manufactured in bulk the first bacitracin and zinc bacitracin in the world. Zinc bacitracin is approved by the FDA for use in ointments, tablets, implantation pellets, suppositories, and troches, either alone or combined with other microbiotics or therapeutic agents. A special grinding process yields zinc bacitracin in any particle sizes required, as fine as 5 to 10 microns. Minimum guaranteed potency: 50,000 units/gram. Immediate delivery.

CSC

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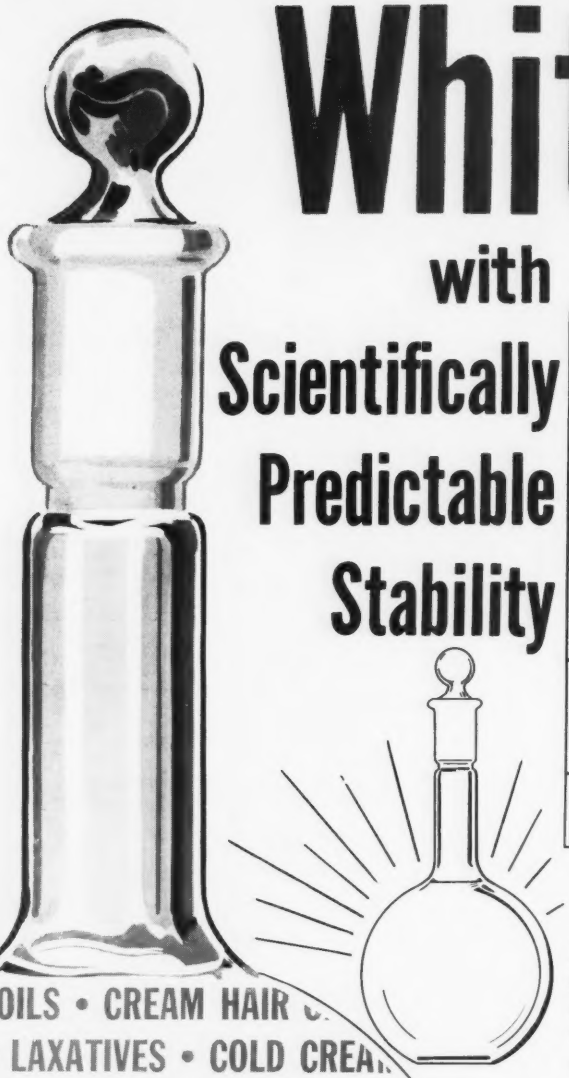
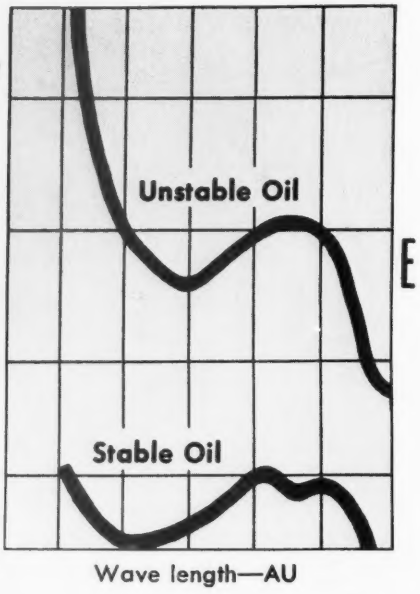
with Scientifically Predictable Stability





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OILS • LAXATIVES • COLD CREA
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Is there an "ideal" enteric coating?

If there were, it would have to be:

inert and non-toxic

A chronic-toxicity study on albino rats, fed diets containing 5%, 20%, and 30% of cellulose acetate phthalate, disclosed no identifiable toxic effects. "In general," concluded the investigators, "cellulose acetate phthalate seems to be remarkably inert as a compound of the diet."

easy to apply in a continuous, imperforate, sturdy coating

Eastman C-A-P Cellulose Acetate Phthalate lends itself readily to conventional coating procedures. It is promptly soluble in many organic solvents, singly or in combination. Coatings properly applied are smooth, glossy, and continuous.

completely resistant to chemical action of the gastric juices and to erosion from stomach motion

In one investigation, tablets coated with C-A-P showed no signs of disintegration after seven days in a continuously-agitated artificial gastric juice. The coating averaged 0.4 grain on each 5-grain tablet—a trifle less than 10%.

promptly and completely soluble in the upper intestine

In the same investigation, tablets coated with C-A-P were tested in two types of artificial *intestinal* juice, with constant mechanical stirring at 37 C. In juice with a pH of 8.5, all tablets disintegrated within 50 minutes. In juice with a pH of 6.9, all tablets showed evidence of rupture in 70 to 75 minutes.

Tests *in vivo* support the results of *in vitro* tests. The action of C-A-P depends not on the solvent action of water, not on the rate of stomach emptying, not even entirely on alkalinity of the intestine, but on the total chemical climate of the intestine.

Ideal? Close enough? You are the best judge of that. *Eastman C-A-P Cellulose Acetate Phthalate* has already taken more than one billion trips through the stomach on enteric pills and tablets. If you are in the mass-production coating of such articles, this could be a good time to take a look at C-A-P. For a sample, descriptive folder, and procedural bulletin, write to ***Distillation Products Industries,*** Rochester 3, N. Y. Sales offices: New York and Chicago • W. M. Gillies, Inc., West Coast • Charles Albert Smith Limited, Montreal and Toronto.

"Eastman" and "C-A-P" are trademarks

DPi

Also ... vitamins A and E ... distilled monoglycerides ... some 3700 Eastman Organic Chemicals for science and industry

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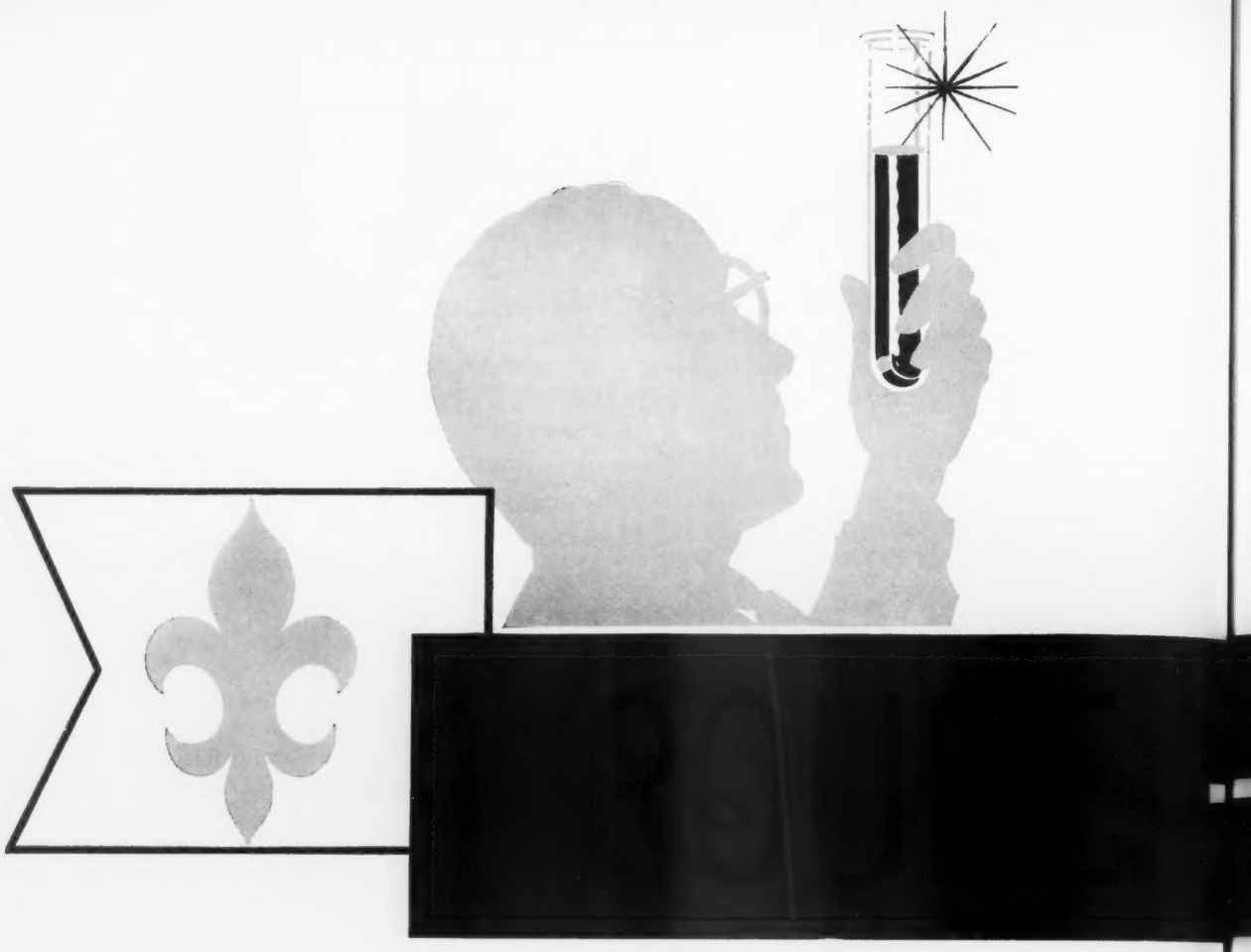

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Their creative genius is attested by the many proven international successes in the field of fragrance requirements . . . be it in the development of original perfumes, colognes, aerosols, cosmetics, soaps and other toiletries . . . or in the masking area where odors have to be covered rather than developed.

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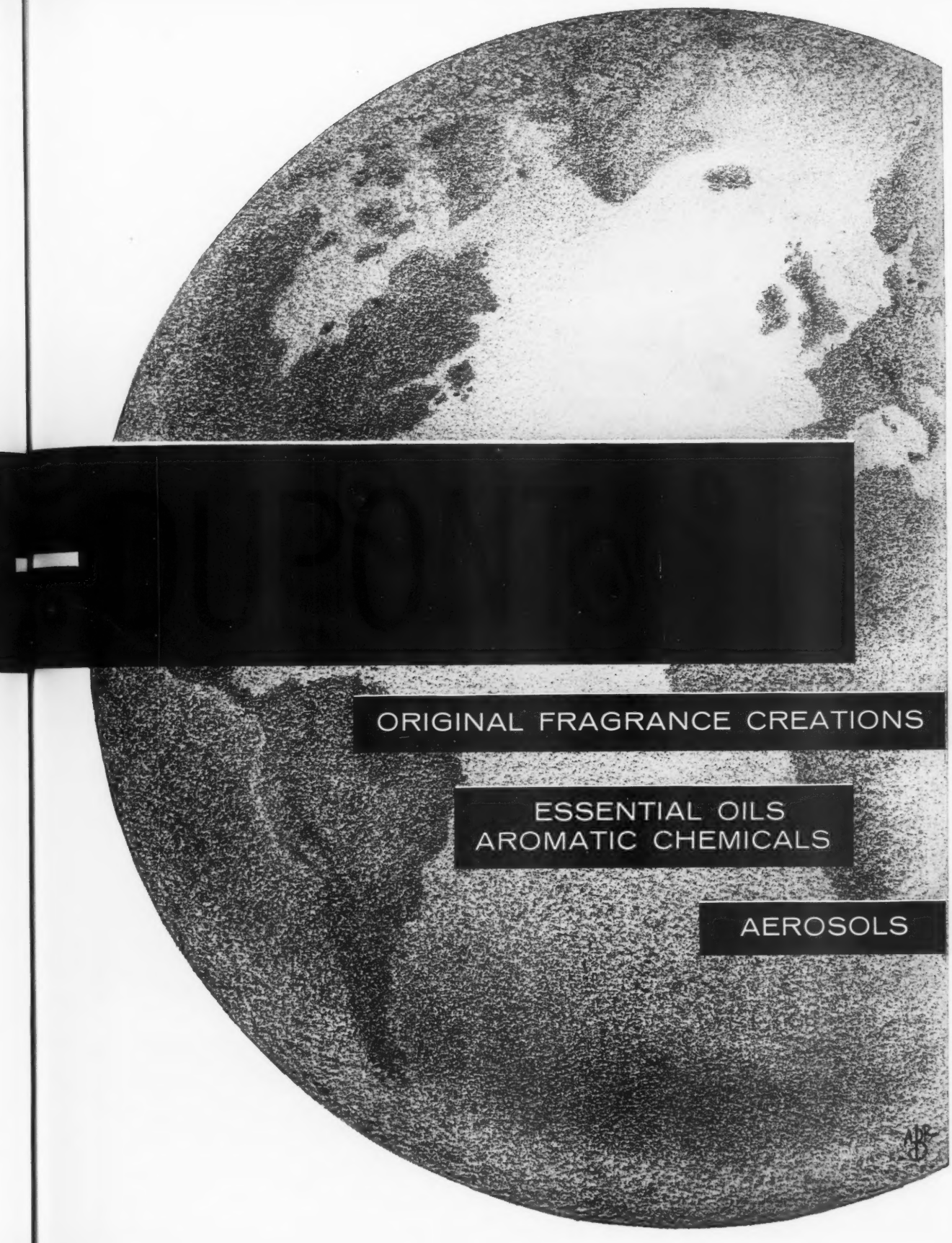
ORIGINAL FRAGRANCE CREATIONS
ESSENTIAL OILS
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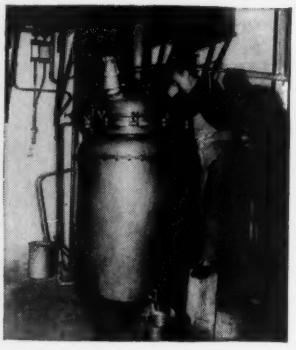
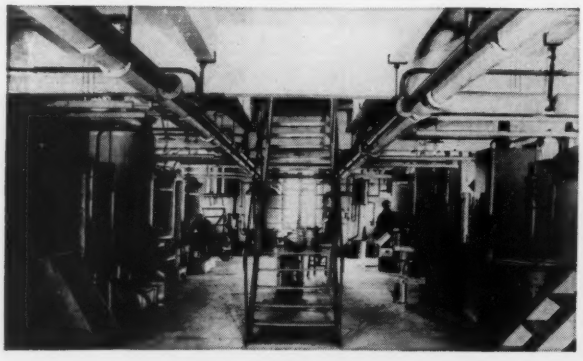
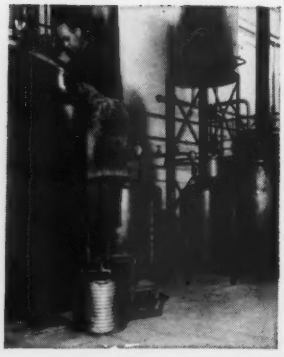
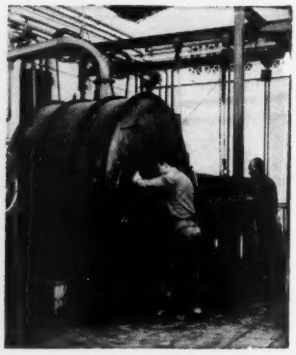
AEROSOLS

CAPACITY



QUALITY

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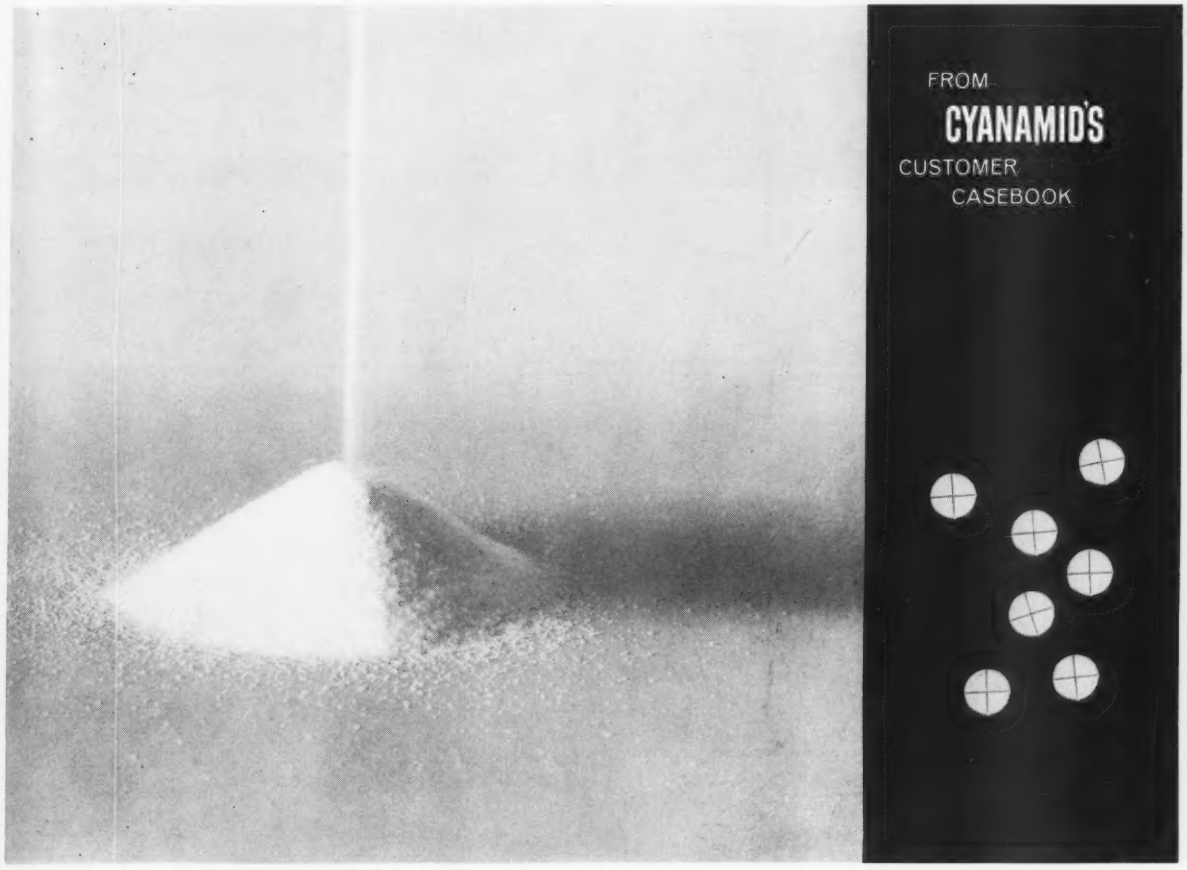

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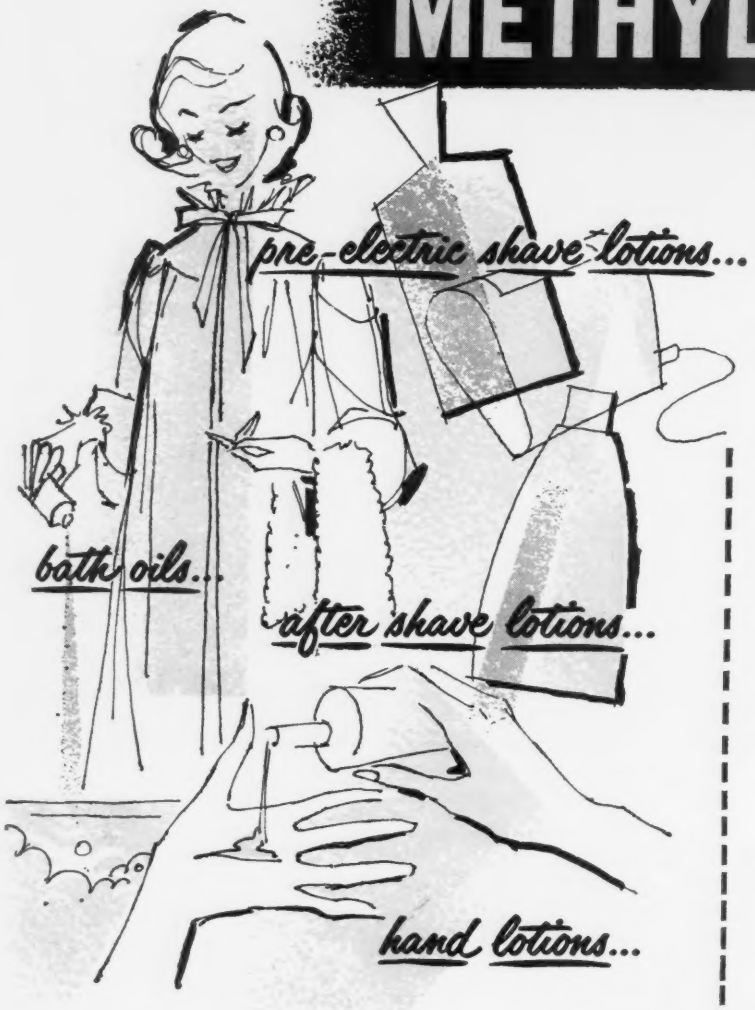

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Our laboratory tests indicate that the new Stepan purified grades of methyl myristate, methyl palmitate and mixed C_{16}-C_{18} methyl esters have definite possibilities for use in the cosmetic field. They impart the same, smooth feel to the skin as do isopropyl myristate and isopropyl palmitate yet the corresponding methyl esters are considerably lower in price. An independent laboratory has indicated that they are non-irritating and have no allergenic reaction based on their tests. We will be glad to send you copies of these test results.

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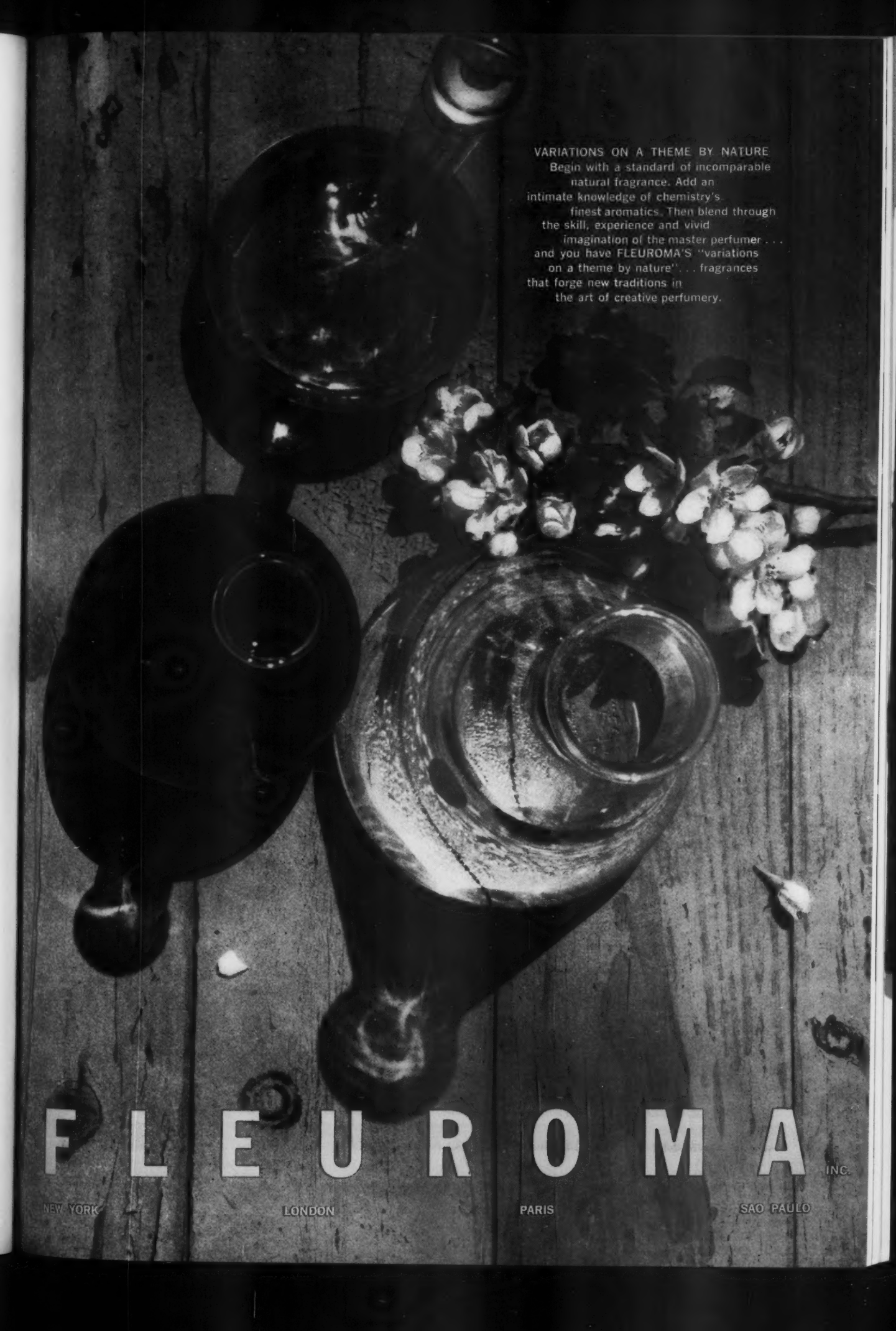
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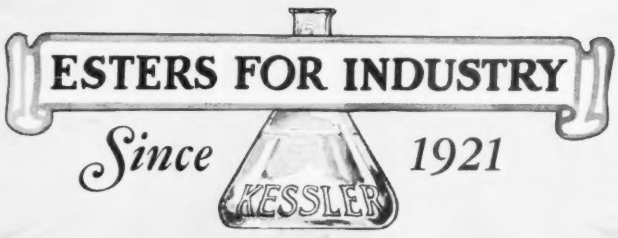

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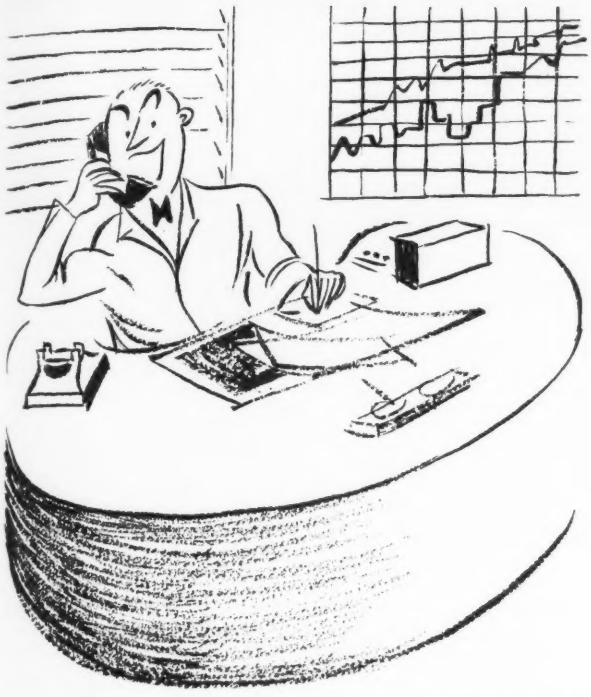

"Tell the research department to get on the ball—our placebos are outselling their wonder drugs."

Keeping Posted

Lilly and Syntex Research

Eli Lilly and Company and Syntex Corporation have signed a cooperative research agreement under which Lilly will share the expense of Syntex research and also will conduct clinical investigations of promising new compounds discovered in the Syntex laboratories. Products resulting from this research will be available for marketing by both companies. In a joint statement, Eugene N. Beeseley, Lilly president, and Dr. George Rosenkranz, Syntex president, said:

"Lilly's contributions through this agreement should help speed the development of important new drugs and result in wider distribution of Syntex-discovered compounds. The scientific role of Syntex also will be strengthened through research cooperation, particularly through the services of the Lilly Clinical Research Laboratories. Challenging possibilities are also presented in the field of agricultural and veterinary research."

Dr. Thomas P. Carney, Lilly's vice-president for research, development, and control, praised the quality of Syntex research: "Syntex employs more than 100 scientists on steroid research alone. Syntex has pioneered in this field. The outstanding ability of their scientists, the significance of their past discoveries, and their impressive contributions to the scientific literature are recognized everywhere. We shall be delighted to work with them."

Through subsidiaries in Mexico, Puerto Rico, and the United States, Syntex manufactures and sells steroid hormones. This cooperative venture puts Lilly into the steroid field for the first time.

Colgate Research Center

Colgate-Palmolive Company will establish a multimillion dollar center for basic and applied research of 200,000 square feet on a 75-acre tract purchased from Rutgers University and bordering on the University's science center which is planned to be one of the largest of its type in the country.

Dr. John R. Brown, Jr., Colgate vice-president for research and development, said that there is a mutually beneficial interchange of ideas and information between the University's scientists and the staff members of Colgate Laboratory for Dental Medicine Research, already located on the science campus and the company's Biological Research Laboratories, also at New Brunswick. When completed, the new research headquarters will house the biological and dental groups and many other Colgate-Palmolive Research sections. Many of the company's long-range, basic studies will be undertaken there as well as part of its product development work now being carried on at Jersey City.

Ground for the new center will be broken in about eight months and completion of the two-story structure is scheduled for late 1961. Having a glass, ceramic and aluminum exterior with a frontage of 360 feet, there will be two main laboratory wings, each 250 feet long, radiating to the rear from an axis corridor that can be extended to provide for additional laboratory wings. Three smaller wings to the front of the building will be occupied by the administrative sections, an information center with a large library and seminar room, and a cafeteria. The building is designed to accommodate about 375 persons. Plans call for approximately 170 laboratory modules.

Vick Chemical Facts

Reporting for the fiscal year ended June 30, 1959, Vick Chemical shows sales of $115,227,829, up 7.7 per cent from the previous year's $107,042,993 despite lower incidence of colds and other respiratory ailments this year than in 1957-1958, and up 22 per cent from $94,796,434 for 1956-1957.

All major segments of the business increased. Ethical and veterinary drugs sales were up 9 per cent to $48.6 million; proprietary drugs sales were up

There are sales-sparking ideas in the Atlas technical literature prepared for cosmetic formulators. This up-to-date library is full of techniques you can use to add new sales appeal to dozens of kinds of creams and lotions.

The list shown here represents the bulletins we have published in just the past two years. Check them . . . ask for any you'd like to have. And look to Atlas for important contributions, of industry-wide interest, in the art of formulating modern cosmetics.

Guide to the use of SORBO® and surfactants in cosmetics—36 pages

Formulary of typical cosmetic formulations—32 pages

Catalog of Atlas Cosmetic products—12 pages

Atlas Marketing and Technical Service Bulletins on:

Anti-Perspirant Sticks
Silicone Hand Cream
Waterless Hand Cleaners
Aerosol Toothpastes
Suntan Preparations
Nitrogen-Propelled Emulsions
Using glycerol monostearate, Acid-Stable in creams and lotions
Using glycerol monostearate, Non-Self-Emulsifying in soap-free and soap-type products
Emulsions in Flexible Containers

Chemicals Division
ATLAS POWDER COMPANY
Wilmington 99, Delaware

18 per cent to $50.3 million; and chemicals and plastics sales were up 15 per cent to $15 million.

Net earnings, after adjustment for unremitted foreign income, were $12,156,819, an increase of $2,086,580 over the previous year, with $674,769 of this increase accounted for by the transfer of accumulated prior years' profits from the Philippines to the United States to limit exchange losses. Last year's earnings were 21 per cent greater than the previous year's, and 54 per cent greater than earnings for the year before that.

Research expenditures for the past year totaled $4.2 million, with an additional $700 thousand spent to expand research facilities. Three companies were acquired during the year: Walker Laboratories, a vitamin and nutrition pharmaceutical specialties house; The Lavoris Company, manufacturer since 1902 of a leading mouth wash; and Milton Antiseptic, Ltd., manufacturer of *Milton* Fluid, used throughout Britain to sterilize baby bottles.

Sales figures included cosmetic sales for only the first three months of the fiscal year as this business was sold to Chesebrough-Pond's in October, 1958. These three month's sales totaled $1.3 million, compared with $6.4 million for the full 12 months of 1957-1958. Ethical sales (48.6 million), a portion of which came from Walker Laboratories, acquired July 2, 1958, are now considerably larger than the entire sales of the company 10 years ago ($42.6 million).

International sales in 117 countries outside the United States amounted to $25.2 million, compared with $21.5 million last year, doubling the sales of five years ago, and tripling the sales of 10 years ago.

Fair Trade Council Dissolved

The American Fair Trade Council, Inc., is being dissolved following the vote of the members of the 21-year-old organization. John W. Anderson of Gary Anderson, cofounder and long-time president of the AFTC, said that this action was taken to combat confusion and to strengthen the Quality Stabilization educational campaign. He said that "the services of a new organization, Quality Brands Associates of America, Inc., will be made available to AFTC members."

Mr. Anderson said that the development of a new concept of protection of manufacturers' property rights in their trademarks, sponsored by Quality Brand Associates, was a major factor in the decision to concentrate efforts, through QBA, toward the establishment, on a national basis, of the principle of quality stabilization, through price stabilization, of top-value trademarked products. This QBA concept is offered as more effective than the state-by-state contract system of fair trade. Efforts toward enactment of Federal Fair Trade legislation to repair damage now has failed through two sessions of Congress, he said.

"The Quality Stabilization Bill HR 3187, introduced in Congress by Representative Ray J. Madden (D. Ind.), can best be described as property protection legislation," said Mr. Anderson. "It is based squarely and simply upon the proposition supported by the U. S. Supreme Court, that a manufacturer's property right in his trademark does not diminish or extinguish upon transfer of the product to, or by, a reseller. Enactment of this bill would enable a manufacturer to stop—quickly and effectively—damaging abuses of his brand name or trademark. The bill specifically cites three reseller practices—bait advertising, price manipulation, and consumer deception —which 'trespass' on the manufacturer's property.

"Under Quality Stabilization, violation by a reseller can be stopped by the manufacturer by simply revoking the reseller's right to use the manufacturer's brand name or trademark in advertising or selling the product."

Vitamin B_{12} Price Cut Again

The price of crystalline vitamin B_{12} was cut again last month, this time by 14 per cent from $139 per gram to $120 per gram. While this price cut was not as sharp or dramatic as some of the others, it serves to indicate that lower costs resulting from increased volume and/or depreciation of existing facilities or new raw materials and processes is passed on to those who use the important products of the drug industry.

In October, 1949, we reported that the price per milligram had been dropped over 40 per cent from $11.50 to $6.50. This meant a drop per gram from $11,500 to $6,500; and per kilogram, from $11,500,000 to $6,500,000.

In October, 1951, we reported another drop from $450 to $350 per gram; or only $350,000 per kilogram. We found that the price per kilogram is only $120,000.

Although this vitamin might seem high as chemicals go, the infinitesimal amounts used in treatment of disease, make its use as a drug in treatment extremely low. The amount used parenterally in pernicious anemia is 50 micrograms twice a week, and then only 50 micrograms once a week, making the cost for treatment only from $0.012 to $0.024.

Fair Trade and Drug Prices

The Bureau of Education on Fair Trade has made an interesting study entitled Fair Trade and Drug Prices. This study, from which we will quote, is, so far as we can determine, not of major importance as to whether or not more effective fair trade legislation will be enacted. While fair trade has been of prime importance to manufacturers of drugs and cosmetics, as well as some other industries including book publishers, we have never felt that fair trade as applied to these fields caused its breakdown. After all there is a wide range of prices for competitive drugs and cosmetics, and fair trade in these fields certainly does not unduly penalize the average buyer.

Replica of perfume bottle used in the year 1768

SINCE 1768 the House of Chiris has dedicated itself to the Fifth Sense. In the development of Essential Oils, Floral Absolutes, Chemical Isolates, Synthetic Chemicals, and all those creations and specialties which combine industrial aromatics with natural products and produce fragrance, the House of Chiris has a cherished history. Today Chiris maintains laboratories headed by experienced chemists who have available to them not only the accumulated knowledge of generations of Chiris perfumers and chemists, but also the research facilities of five modern laboratories located in Grasse and Paris, London, Sao Paulo (Brazil), and New York City. Whether Essential Oils, Isolates, or combinations thereof, are used as fragrance constituents by the perfumery, soap, cosmetics or allied industries, we are happy to be consulted.

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It was the attempt to apply fair trade to large and costly appliances and other items where cut prices represented the saving of a considerable number of dollars that really caused fair trade's breakdown.

International Cosmetic Chemists

The International Federation of Societies of Cosmetic Chemists became a reality last September 8, with the election of Maison G. de Navarre of the Society of Cosmetic Chemists of the United States as its first president, and the appointment of a working committee consisting of Dr. R. H. Marriott of England, Dr. L. W. Masch of Germany, and Doctor P. Velon of France. Eight countries were represented at the meeting held September 7 and 8, and the new Federation will include the Societies of Belgium, Switzerland, Germany, England, France, Spain, and the United States, whose representatives attended the meeting, and also Denmark and Italy, who were not represented. Societies of other countries are said to have expressed an interest in the new Federation. Sabbat J. Strianse, chairman of the International Affairs Committee, who also represented the American Society, reports that work has begun on a new constitution and that many of the points upon which there was disagreement are being worked out.

Drug, Chemical and Allied Trades Association

The Drug, Chemical and Allied Trades Association is the new name of the Drug, Chemical and Allied Trades Section of the New York Board of Trade. While the DCAT, or the association, remains a section of the New York Board of Trade, it now has a name which gives the impression that it is a separate entity, and that seems to be the general idea. It will be recalled that a year ago, the name of the chief executive officer of this group was changed from chairman to president. This was part of the same general plan. Since there were various committees of DCAT with their chairmen, it was thought that the chief executive officer of the group should be called the president.

What the next step will be is anybody's surmise, but there are some indications that within three years, the Drug Section, or the DCAT, as it has been called, will be an independent association. There are many who are of the opinion that this organization can better afford to stand on its own two feet than be a member of New York Board of Trade.

The DCAT Association has about 800 company members, both small and large. However, a fairly good number of these are out-of-town members who pay less dues than resident members. These members range all over the chemical, drug and related fields, some being firms who perform certain services for large portions of the membership. It is pointed out that the organization has such broad coverage that it would have greater influence in espousing a cause for a segment of membership than if that segment tried to do so through the narrow group of an association of its much smaller group.

Dues for members of all sections of the New York Board of Trade are paid directly to the New York Board of Trade. Money is then allocated by the Board to its various sections for their expenditures. However, over the years, the DCAT has been able to increase its activities to its members by use of the money acquired each year as profits from the annual dinner which some 2,400 men now attend at a price of twenty dollars each. Incidentally, this dinner first took place in 1927 when Charles L. Huisking, father of William W. Huisking, just elected president of the association, was chairman. The idea of the dinner at that time was to bring together once a year a large number of men who did business over the phone throughout the year and who did not see each other very often, if at all. At the first dinners attendance was not over 300 men.

Norwich Expanding Research

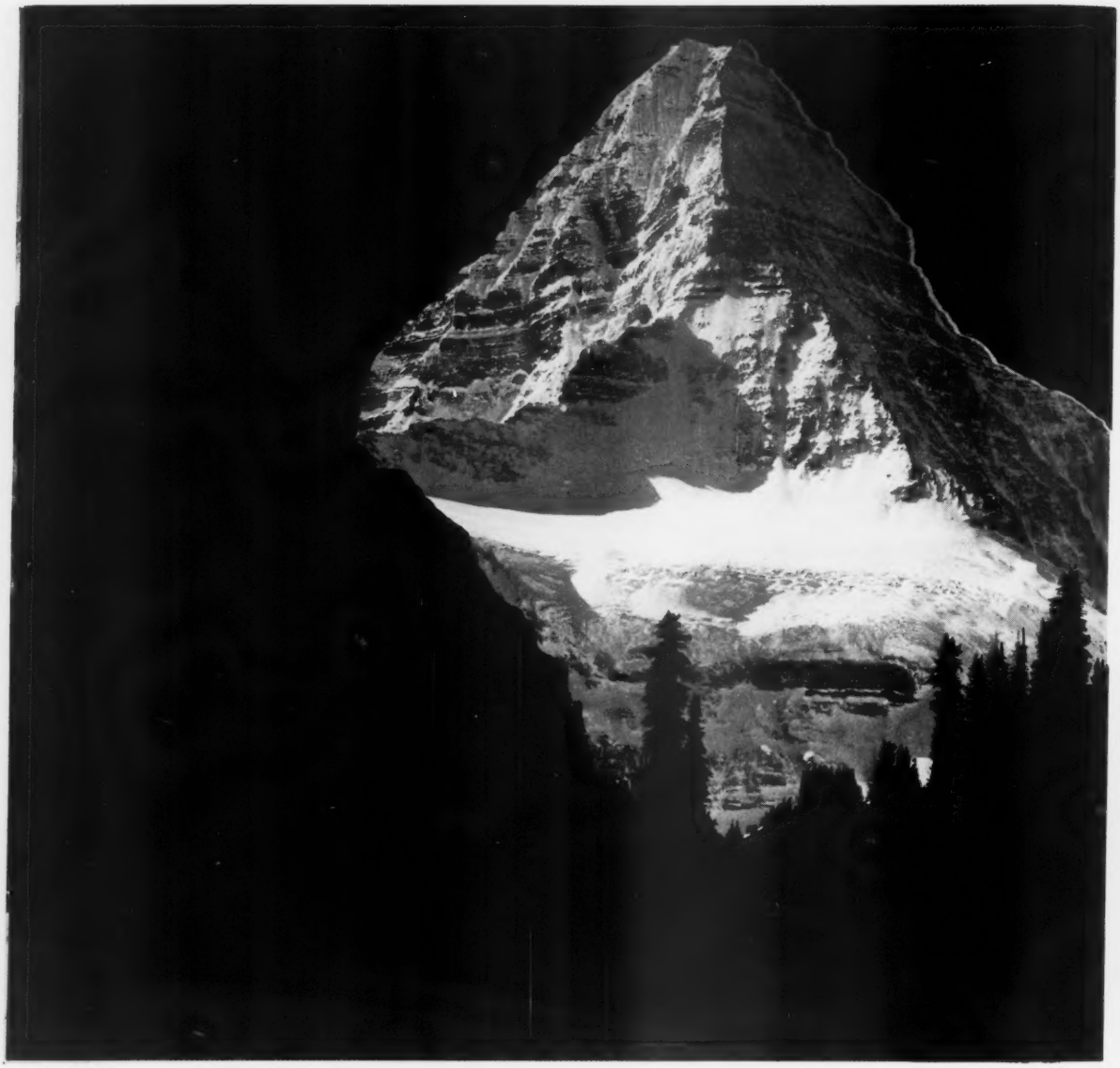
Norwich Pharmacal Company research facilities are to be expanded by an addition to the present building (now comprising 38,800 square feet) two and one-half times the size of the present building. Research facilities at the main plant and at their major location just outside of Norwich have reached maximum capacity as scheduled under an existing plan established five years ago.

"This new research expansion program," stated president George W. Bengart, "will accommodate approximately twice as many research personnel as we have currently. We expect to double our research staff over the next five years."

The building program—to be completed by January 1, 1961—calls for a two-story addition to the northern end of the present structure which will contain expanded sections for pharmacology, pathology and animal work on the first floor, with a medical and research library, offices for medical, veterinary and scientific information personnel, cafeteria, kitchen and photography laboratory on the second floor. The second floor is designed so that it can easily be converted to laboratory space if necessary. An addition will be built to house the pharmaceutical research division now located at the main plant. The microbiology and chemistry wings will also be expanded, and also the present biochemistry section.

The Cost of Medicines

Parke, Davis president Harry J. Loynd told the National Association of Retail Druggists that the pharmacists of the nation should expand and improve the scope and quality of their services as a measure to offset public resentment caused by the "misconception" about the high cost of medicines. Accelerated and broader public knowledge of medicine and medical care, coupled with the fact that "no one likes to buy drugs," has made the cost of medicines



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the target of public and government criticism, he said, adding that complacency by druggists in not responding to these changes in public attitude could mean further federal legislation and further inroads into the pharmacists' merchandise lines by supermarkets, door-to-door salesmen and other retail outlets.

Mr. Loynd told the druggists that they must convince the public that it can obtain a preferable and better service in drug stores, and "emphasize the fact once again that in the majority of cases the purchase of drugs may be one of the biggest bargains of their lifetime." He said that against 4.7 per cent of disposable income spent 20 years ago for all types of medical care, only 4.6 cents of every dollar is spent today for much better medical care. During the same period the proportion of the medical care dollar spent for prescriptions has declined almost 5 cents—from 18.3 cents in 1939, to 13.9 cents.

Mr. Loynd advised that it be admitted that drugs cost too much, but at the same time pointed out that taxes are excessive, building costs are too high, some wages are too high, and many services are too high, and further stated that automobiles, cigarettes, gasoline and entertainment costs are excessive. When it pointed out that some of these are luxuries and that drugs are essential, then point out that foods—meat, potatoes, milk, bread and many other essential things are too high. Concluded Mr. Loynd:

"Let me remind you of a few established facts from the U. S. Department of Labor Consumer Price Index. Since 1945, the period during which penicillin, the sulfa drugs, Chloromycetin, polio vaccine, and many other drugs which have revolutionized medical treatment were introduced, the cost of living has advanced approximately 60 per cent. The cost of food, among things essential to life, increased 74 per cent. But in this same period of major therapeutic advances which have prolonged our life expectancies and reduced or prevented major illnesses, the cost of drugs and prescriptions has increased only 37 per cent."

Health Information Costs

The Health Information Foundation reports that it received contributions totaling $467,650 in 1958. This added to interest of $14,809.79 on government bonds produced total income for that year of $482,459.79. Expenses for the year 1958 were: General and Administrative, $110,960.71; Public Education, $127,722.08; and Research, $283,805.33. These amounts, less refund of $218.84 for research expenses paid out in prior years, totaled $522,269.28, producing an excess of expenses over income for the year of $39,809.49. The fund balance at the end of 1958 totaled $700,924.61 of which $200,000 represented the reserve fund, and $500,924.61 represented funds available for general purposes. These funds were represented by cash of $60,874.61; U. S. Government securities of $639,625 (market value of $609,937.50); and airlines deposit of $425.

Chet Shaw Quitting HNI

Chet Shaw is resigning as executive vice-president of the Health News Institute effective December 31, 1959, a position which he has occupied since the founding of HNI early in 1956. This would seem to indicate that the HNI will be taken completely under the wing of the Pharmaceutical Manufacturers Association which has been paying the major part of its support. Also since the PMA now has a paid president and is moving in the direction of greater public relations activities in the association itself, it seems reasonable to presume that the HNI will be completely under the direction of the PMA.

Abbott Plant in Kansas

With the exception of a Radio-Pharmaceutical Division at Oak Ridge, Ten., Abbott Laboratories is planning the first manufacturing in the United States away from the company's North Chicago headquarters. The plans are for a small chemical plant for production of cyclochexylamine at Wichita, Kansas. Cyclohexylamine is an intermediate used in the manufacture of Sucaryl, the sweetener, and the site was selected because it is a source of inexpensive hydrogen obtained from the Frontier Chemical Company adjacent to the Abbott property. The intermediate, made by combining aniline with hydrogen, will be shipped by tank car to North Chicago, or by drum to other users. The new operation will not affect present chemical manufacturing at North Chicago where a large new chemical building was completed in 1958, and where there is room for expansion.

"Although this is a modest beginning in Wichita," said Floyd K. Thayer, vice-president in charge of Chemical Marketing, "we hope to expand our chemical operations as time goes on, particularly in producing quality chemicals which require hydrogenation."

Product Liability

With the continuing flood of thousands of new products, consumer protection supplementing the work of the Food and Drug Administration is urgently needed, says Alfred S. Julian, immediate past president of the National Association of Claimants' Compensation Attorneys. This statement was made in a report to NACCA in connection with the association's Product Liability Exchange established a year ago to serve as a source of information not only to NACCA lawyers, but also to physicians, legislators, and others interested in public health and safety. In the report it was noted:

"Files of the Exchange now contain information and records of pending legal action on more than 400 products, many of them newly arrived on the market. More than 1,000 lawyers utilized the Exchange in the first twelve months of its existence."

In product liability cases, cosmetics, food and ma-

chinery are the busiest categories, with exploding bottles being the single most reported area. The report declared:

"A drug or cosmetic may be, by its nature, innocuous and even useful, yet, be harmful to people allergic to it. This minority, however small, deserves to be protected from possible injury or death. Proper labeling of products would further eliminate law suits."

Pitman-Moore Tissue Culture Center

Pitman-Moore Company biological laboratories near Zionsville, Indiana, will include a new $1.5 million tissue culture center to be erected. Because of special features, many of which are based on recommendations by outstanding scientists and new requirements of the U. S. Public Health Service, it will be the first of its kind in the country, according to Kenneth F. Valentine, Pitman-Moore president, who added that it will house the development and production of biological products utilizing the tissue culture method.

Dr. S. R. Bozeman, Pitman-Moore vice-president and director of the biological laboratories, says that the new center will be in three separate sections designed so that no material in the production stage will cross its own path during the process. The sections will include areas with facilities for production of the media, the actual production of vaccine, testing and pooling of the product.

Pertussin Product Line

The trademark, Pertussin, is to be extended to cover a full line of cold and throat products, instead of just a cough syrup, as it has for so many years. Two new products to carry this famous trademark will be Pertussin Medicated Vaporizer, and Pertussin Antibiotic Throat Lozenges.

Under the direction of Chesebrough-Pond's, now owners of Pertussin, these two new products have been created to give the entire Pertussin brand an aggressive new image. The new throat lozenges contain four medicated ingredients: antibiotic, antibacterial, anesthetic, and antihistamine, and are said to relieve pain and irritation of sore throats and coughing due to colds. The pertussin medicated vaporizer, packaged in an aerosol spray container, is for relief of the nasal stuffiness and congestion of colds.

T.G.A. Scientific Meeting

The Toilet Goods Association Scientific Section will hold its mid-winter meeting December 1, in the Sert Room of the Waldorf-Astoria Hotel, New York. The meeting will begin at 9:30 A.M., with luncheon in the Empire Room at 12:30. Papers to be presented before the meeting include: The Synthesis and Properties of Mercaptans having different Degrees of Acidity of the Sulfhydryl, by J. W. Haefele, R. W. Broge, and W. L. Courchene of Procter & Gamble; Instrumental Evaluation of Citronella Oils and Oil-Geraniol Citronellol and Other Constituents, by James A. Rogers Jr., director, Instrumental Laboratories, Fritzsche Brothers; Panthenol in Cosmetics, by S. H. Rubin and L. Magid, of Hoffmann-La Roche; The Objective Measurement of Odor III Breath Odor and Deodorization, by Donald A. N. Mackay, Ph.D., David A. Long, Ph.D., and Murray Berdick, Ph.D. (Doctors Mackay and Berdick are respectively associate research director and coordinator of research of Evans Research & Development Corporation, and Dr. Long is senior chemist of American Chicle Company); Recent Advances in Instrumental Examination of Fragrance Materials, by Ernst T. Theimer, Ph.D., director of research, van Amerigen-Haebler, Division of International Flavors & Fragrances; Method for Protecting Peroxide Bleached Human Hair, by Peter Flesch, M.D., Department of Dermatology, University Hospital, University of Pennsylvania; Methionine in Cosmetics and Pharmaceuticals, by Dr. H. J. Prebluda of U. S. Industrial Chemicals Co., and Irwin I. Lubowe, M.D., of Metropolitan Hospital Center of New York Medical College.

Miles Buys Dome Chemicals

Miles Laboratories has acquired Dome Chemicals, New York producer of dermatological pharmaceuticals for the medical profession, for $7.5 million. Dome will be operated as a wholly owned subsidiary of Miles, and will be headed by Irving Wershaw, who, with his wife, Lona Duval, founded Dome, as president and chief executive officer, as well as a vice-president of Miles. No changes in Dome operations or products are planned. The cash purchase was financed largely by short-term borrowing, with permanent financing to be arranged later. Dome Chemicals had net earnings of $428,000 for the first eight months of 1959, compared with $359,000 for all of 1958, and $241,000 for all of 1957. Dome products will be marketed overseas through Miles' international organization which has seven branch plants and operates in more than 100 countries.

Hudnut Has Neutralizer Trouble

Last month the Richard Hudnut Company received complaints that the neutralizer in its Fashion Quick Home Permanent Wave had caused eye irritation in a relatively small number of instances even though the package clearly stated that the neutralizer must be kept out of the eyes. Furthermore, it is said that the neutralizer had been thoroughly tested without any incidents of irritation. It was only after the product was in use by the public that adverse reports were received.

Working closely with the Food and Drug Administration, the company immediately produced a new neutralizer and requested all its trade outlets to set aside their stocks pending replacement of the shampoo neutralizer contained in the original container.

THE PHARMACEUTICAL FUTURE*

BY JOHN J. TOOHY E. R. SQUIBB & SONS

The future of the industry might for convenience, even at the risk of oversimplification, be discussed in two parts: (1) the medical products which the industry will procure and provide, and (2) the extension and improvement in the administration of health services through education and distribution.

The general nature and purpose of the drugs of tomorrow can begin to be seen in the unparalled investigative work that is now going on in manufacturers' research laboratories, in universities, in private laboratories, and in the vast programs planned for governmental research, which in this country is receiving unprecedented support from the Administration and Congress, reflecting the will of the people.

The immediate targets concern the cardiovascular field with its grim record of mortality through coronary disease, atherosclerosis, strokes, and hypertension; the many-sided problems of cancer, arthritis, and the metabolic diseases; the vast potential in mental disease, where pyscho-pharmacological drugs are finding great promise in behavior patterns, and in establishing disease categories; the acute allergies, infectious and viral diseases; and important areas of neurological and opthalmic diseases.

Constant analysis of the needs of the professions, penetrating study of incidence of disease and appraisal of available products and procedures point out the road ahead for new product research, and for product and process improvement.

For some of these conditions, we are beginning to see early glimmerings of products which are useful and effective under limited conditions, a far cry from the recent past where there was little or nothing specific. It is tempting to set a timetable for the emergence of "breakthrough" drugs in these important disease areas, for instance, the prediction of an all-purpose cancer drug within five or ten years.

There is, however, no way of foreseeing the twists and turns that research pathways may take as biological knowledge advances. For instance, the significance of cholesterol serum level in atherosclerosis is now roundly debated, and the tremendous butter surplus may be eased. Certainly it is impossible to anticipate the happy accidents that occasionally fall to prepared minds as they have in the past, and spark evolutionary developments, which the public relations man naturally translates into "revolutionary developments." In addition to the empirical search that follows intelligent leads, there is renewed interest in basic studies which teach the how and why and examine mechanisms of immunity and susceptibility. They shed helpful light that can advance our frontiers and close in on the core of the target.

It is almost certain that the sheer weight of empirical examination of leads, behind a scientific plan, will turn up many useful agents in cancer, and in other fields. Some of these breakthroughs will arrive in clusters, close behind one another, and platform speakers at another forum like this, will talk of a new era in medicine, as we now think of the antibiotic era, or the steroid era.

With advances in cell chemistry, new developments in peptide and protein chemistry, the precise differentiation of physiological cause and effect, continuous front-line research will uncover new drugs for the control of diseases. Conditions we now refer to as "vague symptoms" will be named and defined, and answered, not alone to correct illness, but to seek out the pathways to the fullness of good health, as distinct from disease entities.

A significant renaissance of biological agents has been moving in, with the glorious victory over polio, and now gives the pediatrician a precious preventive program with a four-way combined vaccine—DTPP. The riddles of virus diseases will clear up, one by one, and some of the immunizing vaccines may become as compulsory as small pox. Radio-isotopes al-

(*Continued on page 565*)

*Presented before the Pharmacy Education-Industry Forum, Princeton, N. J.

EVERETT L. SAUL, CHAIRMAN

SCC SEMINAR 1959

PERCUTANEOUS ABSORPTION

With the innovation of a single general subject, Percutaneous Absorption, the sixth seminar of the Society of Cosmetic Cosmetics was held at the French Institute in New York, on September 23 and 24. Organized by the seminar chairman, Dr. Everett L. Saul, the sessions attracted almost 300 registrants for the papers, discussions, luncheons, cocktail party, and dinner. All of the sessions were marked by attentive audiences and vigorous discussion by panels and from the floor.

Wednesday morning papers were devoted to Methods for Measuring Percutaneous Absorption, with Dr. Saul as chairman, and papers by Dr. Saul, "Percutaneous Absorption and the Cosmetic Manufacturer;" Dr. Irvin H. Blank, "Statement of the Problem; Definition of Terms; Critical Review of Past Methods;" M. Ainsworth's paper, delivered by Dr. Kenneth M. Wilson, "Newer Methods for Meas-

Among the speakers at the Cosmetic Chemists Seminar, from left to right: T. Higuchi, A. Rostenberg, Jr., Saul Rubin, B. Choman, Val Cotty, R. D. Griesemer, L. J. Vinson, Max A. Goldziher, Raymond Suskind, F. D. Malkinson, K. M. Wilson, Paul Lauffer, Irvin H. Blank, and Fred Snider. Seminar subject was percutaneous absorption.

uring Absorption;" and Dr. B. Choman's report, "Autoradiographic Studies on Percutaneous Absorption." The discussion panel consisted of the above speakers, along with Drs. Griesemer and Higuchi.

The afternoon group of papers, introduced by Dr. Blank, covered Factors which Influence Percutaneous Absorption, including "Biological Factors," by R. D. Griesemer and "Physicochemical Factors," by Dr. T. Higuchi.

Thursday morning papers were devoted to Percutaneous Absorption of Cosmetic Chemicals Resulting in Favorable Effects, chaired by Dr. Paul Lauffer. "Estrogens" were discussed by Dr. Max A. Goldzieher; "Adrenal Steroids," by Dr. Frederick D. Malkinson; "Salicylates," by Dr. Val Cotty; "Vitamins," by Dr. Saul Rubin; and the panel consisted of these speakers. The final session on Friday afternoon was devoted to Percutaneous Absorption of Cosmetic Chemicals Resulting in Unfavorable Effects, with Dr. Raymond Suskind as chairman. Dr. Suskind discussed "The Appraisal of Cosmetic Materials for Cutaneous Hazard;" Dr. L. J. Vinson, "Percutaneous Absorption and Detergents;" Dr. F. H. Snyder, "Systemic Toxicological Reactions Resulting from Percutaneous Absorption;" and Dr. Adolph Rostenberg, Jr., "Cutaneous Reactions from Cosmetics as Evidence of Cutaneous Absorption." The panel consisted of the above speakers.

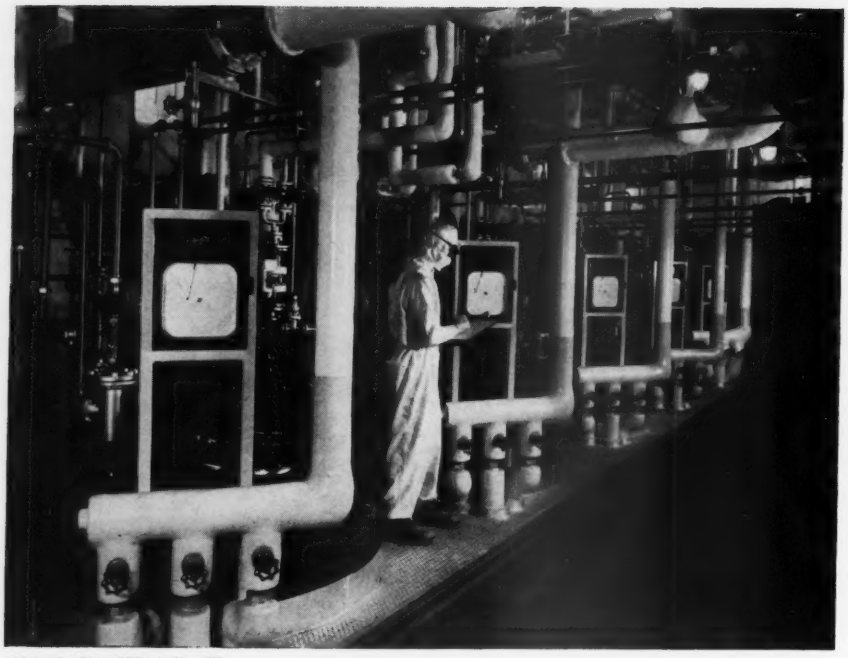
With increasing knowledge, raw materials, methods of measurement and evaluation, according to *Dr. Everett L. Saul* of Bristol-Myers Company, new avenues of approach have become available to the cosmetic manufacturer. He now seeks distinctive products using biologically active substances. While his goal is to provide consumer products which have a more demonstrable value, he becomes more and more involved in problems of side effects, toxicity, irritation, and systemic action.

The systemic action comes about primarily from percutaneous absorption of the ingredients he would like to include in his product. This entire field of investigation must result in redefinitions of cosmetics and drugs, beneficial and harmful.

According to *Dr. Irvin H. Blank* of the Harvard Medical School, we should be concerned, with respect to percutaneous absorption, with trying to determine the movement of molecules out of a cosmetic and into the skin, and attempt to learn at what rate this movement occurs and into which part of the skin the molecules move. A number of "yardsticks" have been used to measure the movement of molecules into the skin. These include penetration into "models" of skin,

(*Continued on page 536*)

Some of those attending the Cosmetic Seminar, from left to right: O. Marton, M. Root, Walter Wynne, A. Newcombe, P. Lauffer, Sophie Plechner, S. B. Mecca, M. L. Rosenthal, George Kolar, P. Bouillette, G. Karsch, K. Russell, H. Henken, M. G. deNavarre, M. Schwartz, G. Fiedler, R. Schuler, I. Malmstrom, S. Gershon, W G. Fredell, Agnes Corte.



COURTESY CHAS. PFIZER & CO., INC.

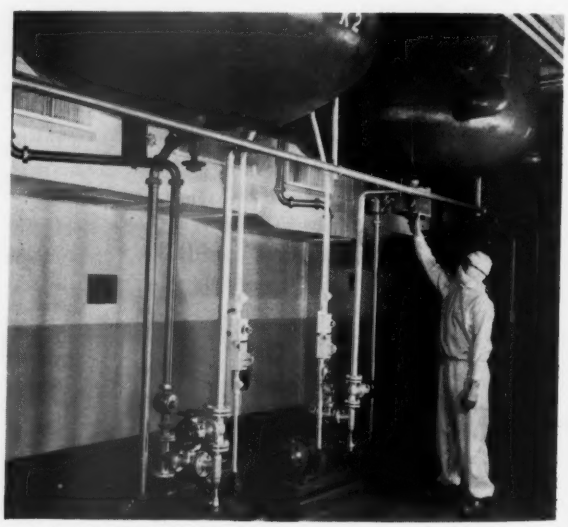
PHARMACEUTICAL FERMENTATIONS, 1958*

BY SAMUEL C. BEESCH AND FRED W. TANNER, JR. CHAS. PFIZER & COMPANY, INC.

Despite the economic problems of 1958 and the lack of epidemics such as the Asian flu outbreak of a year ago, pharmaceutical sales reached new heights. Antibiotics for human medicine alone were valued at $380,000,000, with another $67,000,000 used in animal feeds, veterinary drugs, and other miscellaneous products. By 1965 one estimate expects human needs alone will be valued at $440,000,000, coupled with a substantial increase in nonpharmaceutical uses. Since the war, and widespread use of antibiotics, the average death rate caused by eight infectious diseases has been reduced by 58 per cent, with tuberculosis leading the way at 78 per cent.

A second economic analysis of the drug industry estimates antibiotics sales in 1958 at $431,000,000; steroid hormones, $140,000,000 (with corticoids accounting for $95,000,000 and sex hormones, $25,000,000), and vitamins, $250,000,000. Thus, these three classes comprise $800,000,000 of the total ethical and proprietary market of $1,900,000,000 in sales. The wonder drugs of the 1930's, the sulfas, still command $42,000,000. Anticancer agents from microorganisms in the future may comprise another important group of products if the current explorations are successful.

Certain other products, such as organic acids, have continued their growth. A domestic producer has announced plans to increase production facilities for



COURTESY CHAS. PFIZER & CO., INC.

*Abstracted from **Industrial and Engineering Chemistry**, 51:1086, September 1959. Copyright by the American Chemical Society and reprinted by permission.

EXPANSION IN THE DRUG AND FERMENTATION INDUSTRY

Company	Type of facility	Location	Products
Abbott Laboratories	Research	North Chicago, Ill.	. . . . .
Abbott Laboratories	Mfg.	Sidney, Australia	Fine chemicals, pharmamecuticals
Allen and Hanburys, Ltd.	Mfg.	Tehran, Iran	Pharmaceuticals
Bristol Laboratories (Bristol-Myers Co.)	Research	Syracuse, N. Y.	Cancer research
Carter Products	Mfg.	Cranbury, N. J.	Pharmaceuticals
Carling Breweries	Mfg.	Toronto, Ont.	Beer
Carling Breweries	Mfg.	Atlanta, Ga.	Beer
Federated Pharmaceutical Co., Ltd.	Mfg.	Jamaica, B.W.I.	Pharmaceuticals, antibiotics
Fleischmann Laboratories	Research	Chicago, Ill.	Basic research, quality control
Lakeside Laboratories	Research	Milwaukee, Wis.	. . . . .
Lederle (American Cyanamid)	Mfg.	Gossport, England	Antibiotics, drugs
Lederle (American Cyanamid)	Mfg.	Wellborn, Ont.	Antibiotics
Merck & Co.	Mfg. (tech. assistance to India)	Primpi, India	Streptomycin, dihydrostreptomycin
Merck & Co.	Mfg.	Buenos Aires	Fermentation, steroids
Merck & Co.	Mfg.	India	Vitamins, hormones
Merck & Co.	Mfg.	Cali, Colombia	Antibiotics, hormones
Miles Laboratories	Mfg.	Elkhardt, Ind.	Citric acid
Parke-Davis	Research	Ann Arbor, Mich.	. . . . .
Parke-Davis	Office-mfg.-lab.	Bogota, Colombia	Pharmaceuticals
A. H. Robbins	Research	Richmond, Va.	. . . . .
Schering Corp.	Research	Union, N. J.	Biochem. pilot plant
Schering A. G. (Berlin)	Mfg.	Japan	Pharmaceuticals
E. R. Squibb & Sons (Olin Mathieson)	Mfg.-distribution	France	Pharmaceuticals-distribution
Syntex	Research	Mexico City	. . . . .
Upjohn Co.	Mfg.-distribution	France	Pharmaceuticals-distribution
Upjohn Co.	Mfg.	Bogota, Colombia	Upjohn Products
Upjohn Co.	Mfg.	Johannesburg, S. A.	Upjohn Products
Upjohn Co.	Research	Kalamazoo, Mich.	. . . . .
Warner-Lambert	Mfg.	Villawood, Australia	Cosmetics, pharmaceuticals
Western Wholesale Drugs, Ltd.	Mfg.-sales facilities	Vancouver, B. C.	Pharmaceuticals
Wyeth Laboratories	Research	Radnor, Pa.	. . . . .

citric acid. Gluconic and ascorbic (an indirect fermentation product) acids are finding wider uses. Isoascorbic acid (also an indirect product) is being used for its antioxidant properties. Vitamin prices, both of fermentation and synthetic origin, continue to decline but with high volume sales. Importation has influenced prices.

Several dramatic new types of corticosteroid hormones have broadened the market and increased competition. Fluorosteroids were quickly followed by potentiation effects accomplished by properly placed hydroxyl or methyl groups in their architecture.

Industry surveys outside the United States show a progressive state of development in the antibiotics industry of Europe, as well as Russia and its satellites. There is reason to believe that Soviet-produced antibiotics will be weapons of economic and political influence. Substantial increases in production can be expected from these countries.

The microbe is entering lustily into a new field, that of amino acids: L-lysine of fermentation origin is now supplied in food, pharmaceutical, and feed grades, and L-glutamic acid may be expected to compete with the more classical sources.

Yet, production efficiency gains appear to be paral-

(*Continued on page 557*)

COMPANY ACQUISITIONS

Parent companies	Products	Acquired companies	Products
Allied Laboratories	Drugs	Campana Sales Co.	Proprietary, cosmetics
Bard Pharmaceuticals	Pharmaceuticals	G. F. Harvey Co. (Saratoga Springs, N. Y.)	Ointments
Dumas-Milner Corp.	Household products	Taylor Labs., Inc. (Houston, Tex.)	Drug products
Glaxo Labs., Ltd.	Antibiotics, vaccines	Allen and Hanburys, Ltd.	Pharmaceuticals, insulin
Hampden-Harvard Breweries	Beer	Dobler Brewing (Albany, N. Y.)	Beer
Kingsbury Breweries	Beer	Sioux City Brewing Co. (Sioux City, Iowa)	Beer
Lavoris Co.	Mouth washes	Milton Antiseptic (England)	Mouth washes
Nestle-Lemur	Cosmetics, perfumes	E. L. Patch Co. (Boston, Mass.)	Pharmaceutical specialties
Pabst Brewing Co.	Beer	Blatz Co. (Milwaukee, Wis).	Beer
Chas. Pfizer & Co.	Chemicals, antibiotics	Dumex Co. (India, Ceylon, Pakistan)	Pharmaceuticals, antibiotics, vitamins
Chas. Pfizer & Co.	Chemicals, antibiotics	Kemball, Bishop & Co. (Folkstone, England)	Tartaric, citric, gluconic acids
Plough, Inc.	Drugs, pharmaceuticals	Creolin Co.	Disinfectants
Renfield Importers, Ltd.	Importing Co.	Medley Distilling Co. (Owensboro, Ky.)	Whiskey
Rexall Drug Co.	Drugs	Carnegies, Ltd. (Welyn, London)	Whiskey
A. H. Robbins	Pharmaceuticals	Whittier Labs (Chicago)	Pharmaceuticals
Schering Corp.	Drugs	American Scientific Labs (Madison, Wis.)	Pharmaceuticals
Sterling Drug Co.	Drugs	Delaware Poultry Labs Inc. (Millsboro, Del.)	Veterinary biologicals pharmaceuticals
Vick Chemical	Drugs, chemicals, plastics	Lavoris Co.	Poultry vaccines, animal medicines
Vick Chemical	Drugs, chemicals, plastics	Walker Laboratories (Mt. Vernon, N. Y.)	Mouth washes
			Vitamins, drugs

ESSENTIAL OILS IN ZANZIBAR AND PEMBA

BY ERNEST GUENTHER, PH.D. FRITZSCHE BROTHERS, INC.

The British Protectorate of Zanzibar and adjoining Pemba, tropical islands off the eastern coast of Africa, produce about three-quarters of the world's supply of cloves—one of our most important spices, being employed widely for the flavoring of all sorts of food products and for the isolation of its essential oil.

Cloves are the dried, unopened flower buds which grow in clusters on the terminal branches of *Eugenia caryophyllata* (fam. *Myrtaceae*). The clove tree is a large evergreen, which may attain a height of 30 and even 40 feet.

The clove tree was introduced into Zanzibar in the beginning of the Nineteenth Century and then planted extensively on the holdings of wealthy Arabs. These large plantations are now mostly gone; because of the Islamic law of inheritance they have been continuously subdivided in the course of years, so that now there are thousands of small "shambas" all over the island, a fact, incidentally, that impedes the adaptation of modern and efficient field management.

There are two principal harvests of cloves in Zanzibar and Pemba, that is, the so-called *mwaka* crop (July to September), and the *mvuli* crop (November to January). Harvesting is done by crews of native men, women and children, who pick the clusters of cloves just before the buds open and take them to the processing station on the shamba. Here the harvesters, squatting on the ground, separate the fresh buds from the stems by brushing the clusters with one hand against the palm of the other, clove buds and stems being heaped up separately on coconut mats. This task completed, the foreman or owner of the shamba rapidly measures each workers' output in a pishi, a brass container holding about four pounds of fresh cloves. Payment is made according to the number of pishis harvested by the picker. An experienced worker can collect up to 50 pishis per day, in exceptional cases even more. Wages of harvesting during the past few years averaged about one-half shilling (about seven U. S. cents) per pishi, which means that a good worker could earn up to 25 shillings (about $3.50) per day. It is not surprising that these wages attract many natives from the nearby mainland to participate in the clove harvest of Zanzibar and Pemba as seasonal laborers.

After separation from the stems, the fresh clove buds are spread on coconut mats (or on concrete platforms at the larger plantations) to be dried in the sun. In sunny weather the drying requires four to five days; in overcast weather a longer time is needed. When rain threatens, the cloves must be covered with mats. During proper drying the cloves lose about two-thirds of their original weight. Carefully dried cloves have a bold appearance, a reddish-brown color and a light brown head. Cloves rained upon during the drying process—known as *kokher* cloves—are smaller, somewhat shriveled, and of darker color than sun-dried cloves.

The average yield of dried cloves per tree amounts to about seven pounds but, in an abundant harvest such as that of 1957-58, a large clove tree in Pemba

Clove buds ready for picking, in Zanzibar.

A cluster of freshly picked clove buds.

De-stemming the clove buds, in Zanzibar.

Drying clove buds on a Zanzibar shamba.

may produce as much as 40 pounds. In 1957 the yearly income per tree averaged eight shillings (about $1.12), while the income from a coconut tree was only two shillings (about 28 cents).

The total yearly production of cloves in Zanzibar and Pemba varies greatly, fluctuating between 2,000 and 20,000 English long tons and averaging about 10,700 tons in the last ten years. All-time records with more than 21,000 tons were set in 1937-38 and 1957-58. Pemba supplies roughly 83 per cent and Zanzibar 17 per cent of the total annual output of the Protectorate.

The dried cloves are brought to the warehouses of the Clove Growers Association in Malindi, Zanzibar, where they are inspected, assorted and reinspected before permission for export is granted.

There are three grades of cloves, Grade II being by far the most important one and amounting to about 99 per cent of all clove exports from the two islands.

Grade II must not contain more than 16 per cent of moisture, 7 per cent of *kokher* cloves and 5 per cent of stems, mother-of-cloves, and foreign, superfluous, or inferior matter. Mother-of-cloves are those that have been left longer on the tree and have gone to seed; they are thick and lack a head.

Grade I should really be called "superfine" or "extra;" once used chiefly for temple incense in India, it has not been exported from the islands for a long time.

Grade III is a distiller's grade; but, owing to the small difference in price between Grade II and Grade III, very little of the latter quality is shipped. An importer abroad must guarantee that this grade will be used exclusively for distillation purposes.

Exports of cloves from Zanzibar and Pemba in recent years have been distributed as follows:

(1) Indonesia: about 50 per cent, where the cloves are used chiefly for the flavoring of cigarettes.

(2) India: about 20 per cent, employed mainly in betelnut chew, as well as in temple incense.

(3) United Kingdom and other parts of the world: about 30 per cent, used principally for the flavoring of food products and for the isolation of the essential oil. Unfortunately, exports to the United States, formerly substantial, have declined sharply, owing to the competition of the lower-priced Madagascar spice.

Obviously, the Government of Zanzibar and the management of the Clove Growers Association are not too happy about the distribution of clove exports. The fact that half the exports goes to Indonesia makes for uncertainty: what would happen if the political and economic situation in Indonesia should worsen and lead to import restrictions or payment difficulties?

Another serious problem that has plagued the Zanzibar and Pemba clove industry in recent years is the diseases of clove trees known as "sudden death" and "die-back." A few years ago the former almost wiped out Zanzibar's clove plantations and gravely affected those of Pemba.

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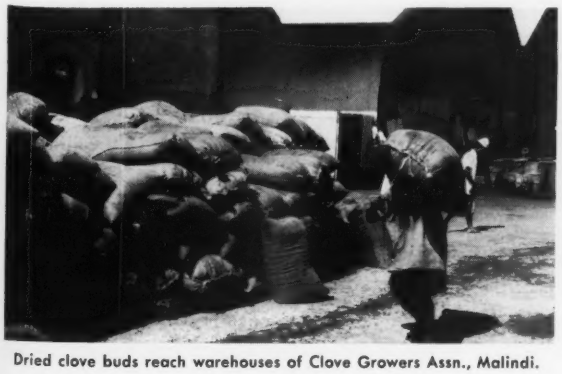
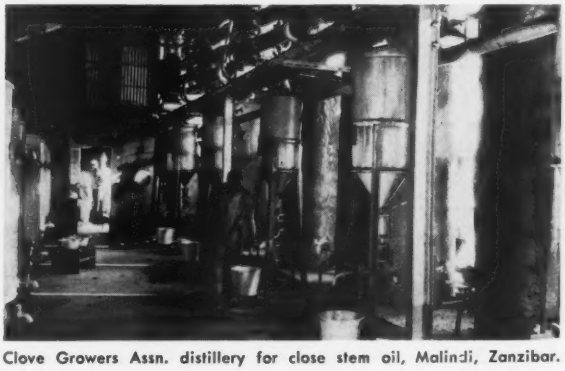
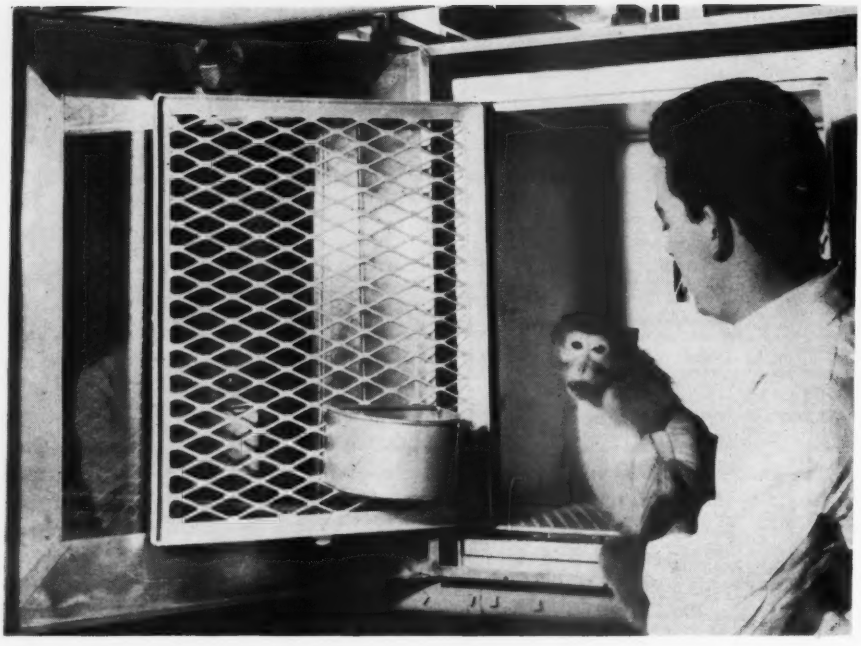


Dried clove buds reach warehouses of Clove Growers Assn., Malindi.



Clove Growers Assn. distillery for close stem oil, Malindi, Zanzibar.



THE ANATOMY OF PHARMACEUTICAL RESEARCH*

BY JOHN T. CONNOR PRESIDENT, MERCK & CO.

My story starts as far back as 1943 when Sharp & Dohme, which through merger later became Merck Sharp & Dohme, decided to launch a basic research project that came to be known as the renal program. It was started because progress in the treatment of certain diseases by chemotherapy was being severely handicapped by lack of fundamental knowledge of how the kidney worked. During the next 16 years the renal program, combining basic research and drug development, produced two major results. First, it produced two medically significant new drugs, along with several times as many that were dismal failures.

More important, however, the program produced such an amount and quality of new concepts about kidney physiology that whole areas of textbook teaching the theory were significantly advanced. Several times during the long evolutionary course of this research new concepts had to be invented before the hunt for the next step could even begin. In fact, this is almost a classic case for the thesis that drugs are first discovered in the mind of man.

*From a paper given before the American Association of Medical Clinics, Chicago, September 26, 1959.

But I am getting ahead of my story. To take charge of the chemical phase of the new renal program, the company chose Dr. James M. Sprague, its director of organic chemistry. To head up the biological phase, the company hired Dr. Karl H. Beyer, then a young M.D. who had earned his doctorate in physiology. He was immediately assigned to work for a short time with a basic research group at Goldwater Memorial Hospital in New York, which was under the direction of Dr. James A. Shannon, now Director of the National Institutes of Health. Dr. Shannon at the time was investigating the renal elimination of sulfa drugs.

After Dr. Beyer came back to the company, one of the first projects he and Dr. Sprague tackled was that of the excessive excretion of penicillin through the kidneys. Many may remember that in the early days we were plagued because as much as four-fifths of this precious antibiotic is eliminated before it can do its life-saving work at the site of infection. Penicillin was then so scarce that it was sometimes extracted from the urine of patients to be used again.

After nearly a year's work, Beyer and Sprague hit

upon an old drug called PAH. It slowed down the excretion of penicillin all right, but it went out through the kidneys so fast itself that it required the ridiculous daily dose of 200 grams to be effective. This was the renal program's first dismal failure.

Though a failure, PAH demonstrated the validity of a new theory. A chemical compound, the group found, could block the secretion of a single substance by the kidney without at the same time blocking the excretion of everything else. They decided to build on this discovery by hunting for a kissing cousin of PAH—one that would block penicillin without being excreted so fast itself.

They concentrated on the sulfonamides—a broad group of chemicals in which the company had had considerable experience. Dr. Sprague probably knew as much about sulfonamides as anyone. He had been awarded the basic patent for synthesizing sulfa drugs of the sulfapyrimidine group. This is the group that includes the most successful of all the sulfa drugs, sulfadiazine.

From then on, over the long course of the renal program, Dr. Beyer and Dr. Sprague held regular Friday afternoon conferences and they were often in daily contact with the other members of their research teams. Such close cooperation between physiology and chemistry hardly exists outside the pharmaceutical industry. Our scientific achievements would be impossible without it.

It took nearly three more years for this new team to produce the next new drug in the program, Caronimide. It turned out to be the second big flop. It was far better than its predecessor, but it brought the inhibitor dose down only to 20 grams a day. But it added one more building block to knowledge of how the kidney worked. It showed that the kidney could do three things to a single compound. It could filter it; it could secrete it through the tubules, and, finally, it could reverse this action and reabsorb it into the blood stream. This was such unorthodox new theory that it was not immediately accepted by the scientific community. In time, the theory came to be accepted and it opened a whole new horizon for renal physiology and therapeutics.

In 1951, nearly eight years after the start of the renal program, The Beyer-Sprague team finally came up with a compound that was effective in inhibiting the excretion of penicillin on a dosage of only two grams a day. The only trouble was that time had robbed the new drug Benemid of much of its charm. It was born too late. During those eight years the industry had learned how to make penicillin so abundantly and cheaply that there was no longer any pressing need for a drug to inhibit its excretion.

So, Benemid became a remedy in search of a condition to relieve. Fortunately for the company exchequer—for eight years can seem a long time to a treasurer to pay and pay when not a single penny returns—fortunately, Benemid found a new condition in serious need of a remedy. Clinical investigators had learned that Benemid affected another mechanism of the kidney, which increased the excretion of uric acid. And excess uric acid retention was one of the effects of gout, which is a chronic, excruciating, incurable disease. Until that time treatment was available only for the acute attack. Since its discovery, Benemid, by maintaining lower uric acid levels, has proved a boon to thousands of persons suffering from this disease.

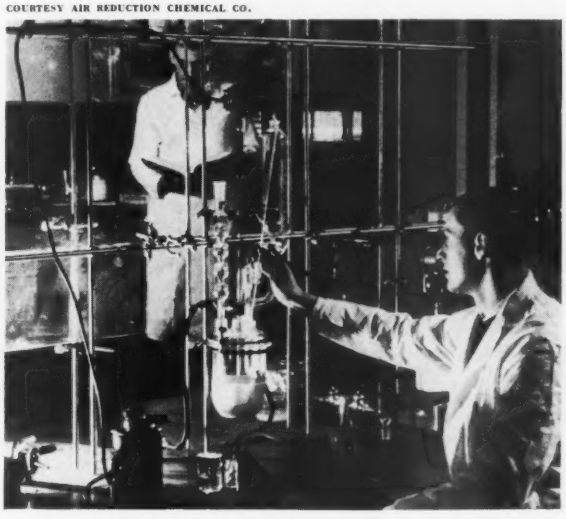
Meanwhile, an important discovery came out of the work of Dr. William B. Schwartz at the Peter Bent Brigham Hospital in Boston. It immediately caught the eye of those working on the renal program. Dr. Schwartz had announced that sulfanilamide showed promising diuretic properties. Thus, it might be helpful in relieving edema, the abnormal retention of fluids in the body that our parents used to call dropsy. Edema, associated with heart failure and other diseases, affected more than a million Americans. It was always debilitating, and often fatal. As you know, clinicians had long been aware of the pressing need for an effective and non-toxic oral diuretic that would relieve edema by increasing the excretion of excess fluids through the kidneys.

Sulfanilamide was far too toxic to be used for this purpose, but Dr. Schwartz did show that a chemical substance could select excess sodium for excretion through the kidneys. As you know, sodium is the villian in edema, since it acts as a binding agent for water. When an excess of sodium accumulates in the body, an excess of water develops. But sulfanilamide had another drawback. It excreted large quantities of bicarbonate along with sodium, thus causing acidosis.

Dr. Schwartz's discovery, plus the pent-up demand of clinicians for an effective and safe diuretic, set off a race between several pharmaceutical companies to see which one could reach the goal line first. Most of

(*Continued on page 567*)

COURTESY AIR REDUCTION CHEMICAL CO.



COSMETIC EMULSIONS

BY JOSEPH KALISH, PH.D.

COURTESY TUSSY

The film laid down on the skin is of interest to the consumer, for it is this film that embodies all of the desired activity and modifying properties expected of the product. This film, as in lipsticks or brilliantines or some liquefying cleansing creams, may be the whole preparation. Where the film should be thin and uniform over a relatively large area, the product can usually be improved by dilution. In this case, an evaporating solvent will permit wider and more uniform distribution of relatively thinner films, as in the case of perfumes and toilet waters, skin toners, deodorants and antiperspirants, nail lacquers, and the like. If the solvent is other than water, as is often the case, its cost may be unnecessarily high in relation to what it does and to the total cost of ingredients; the solvent required may not be compatible with the skin; no satisfactory solvent may be available for the heterogeneous mixture to be applied to the skin. Emulsions with water as a major component are less costly than nonaqueous solutions; water is acceptable to the skin; a film of desired thickness is left after evaporation of the carrier; emulsifying ingredients may improve the quality of the resulting film.

This characterization of an emulsion as primarily a carrier of active ingredients or an aid in the deposition of a desirable film is, of course, neither new nor original. It is stressed, however, to overcome past overemphasis on emulsion character as almost the sole objective in formulation. Enough data and information are now available, especially from the numerous and uniformly high-quality technical brochures provided by raw materials manufacturers, so that the preparation of almost any emulsion should be virtually a routine operation.

An emulsion is a heterogeneous system of two or more phases, usually two liquids, with many of the physical properties of a homogeneous system. A cosmetic emulsion does not readily separate into its components, which remain unchanged chemically, although physical properties of the components may be substantially changed.

One of the liquids is subdivided into small globules, the other is the vehicle in which the small drops move; these are, respectively, the discontinuous and the continuous phases, or internal and external phases. In oil-in-water emulsions, water is the continuous phase; in water-in-oil emulsions, water is subdivided into droplets. Depending upon the total composition of the emulsion, the latter may form a cream or a lotion; emulsions with small proportions of internal phase tend to be more fluid, but modification of the composition of the external phase is usually most important in determining the viscosity of the emulsion. In liquid emulsions, breakdown of the internal liquid into even smaller droplets tends to improve stability.

In classical theory, separation of the emulsion is related to the relative densities of the internal and the

COURTESY HELENA RUBINSTEIN

external liquids—if the droplets are of greater specific gravity, they will tend to settle; if of lower specific gravity, they will tend to move to the top of the liquid. As the diameter of the particles of droplets decreases, they are less affected by gracity. Viscosity of the external phase will also reduce the effect of gravity. Thus, to delay separation of a theoretical emulsion, the internal phase should have a density near that of the external phase, droplets should be of small diameter, and the viscosity of the external phase should also be high. Actually, these theoretical factors will not lead to a stable emulsion if some means is not present to prevent droplets from combining into larger drops. This is an important function of the emulsifying agent, to form a coating or layer around the droplets so that they will not recombine into a large liquid mass. The emulsifying agent, as a surface active agent, also reduces the work required to subdivide the liquid into small particles, making emulsification easier.

Theory, however, does not often enough consider the vital importance of the emulsifying system in modifying the properties of the external phase. Discussions are often limited to the manner in which the electrical charge of the emulsifying agent or the shape and orientation of the emulsifying molecules permit accumulation at the surface of the droplets. Far more important is the manner in which a water-soluble (or dispersible) emulsifier will affect the properties of the aqueous external phase. For example, in an emulsion formulated with 10 per cent of oil, 0.5 per cent of sodium lauryl sulfate, and 89.5 per cent of water, if the average droplet diameter is reduced to two microns, only about one-seventh of the emulsifier molecules will find room on the surface of the droplets to form a monomolecular layer to prevent coalescence, while all the rest will dissolve in the water and affect its viscosity, and other physical properties. Theoretical laws are of little use in formulating cosmetic emulsions, which tend to follow practical rules instead. The general aim should then be to select an emulsifying system that will disperse the internal phase effectively, but will also modify the external phase in a manner favorable to better cosmetic acceptability as well as greater stability.

Cosmetic emulsions may be either creams or lotions, but fluidity is no necessary indication of their internal phase concentration. Products with lower proportions of external phase may be creams, while more concentrated emulsions may be liquids. Creams and lotions may be oil-in-water or water-in-oil; the same general rules apply in both types, but the latter are more difficult to stabilize.

Emulsions are seldom formulated with a single emulsifying agent, since optimum stability is usually attained with mixtures. Surface active emulsifiers usually consist of relatively long molecules, one end of which is attracted to water (hydrophilic) and the other attracted by oils (lipophilic). If the lipophilic character predominates, the compound will be soluble in oils and insoluble in water; the reverse is true if the hydrophilic character is stronger. As a general qualitative rule, water-soluble emulsifiers promote the formation of oil-in-water emulsions, while oil-soluble emulsifiers form the reverse type of emulsion. Some emulsifying agents are powerful interfacial tension reducing agents, others have relatively less effect. The most stable emulsions result from the use of a mixture of emulsifiers with different water solubilities and different emulsifying power. Good creams and lotions result, for instance, from the combination of lauryl sulfates or soaps, which are powerful water-soluble promoters of oil-in-water emulsions, with glyceryl or glycol ethers or esters of fatty alcohols or fatty acids which are water insoluble and, generally, rather poor water-in-oil emulsion promoters.

These general concepts have been neatly summarized and given some quantitative character in Griffin's "HLB" system. Lipophilic emulsifiers have low HLB values, hydrophilic compounds have higher values, and combinations are used to obtain average numbers suitable for specific emulsification purposes. The system brings a degree of order to what otherwise might be the hit-or-miss selection of a suitable emulsifying combination. It is not a substitute for laboratory experimentation to determine the best combination for a purpose.

As chemical compounds, emulsifiers may be either ionized or nonionized. Auxiliaries, for the most part, are nonionized compounds. Primary emulsifiers are nonionics; anionics, in which the bulk of the molecule bears a negative charge; or cationics, with a positive charge at one end of a large molecule. Combination emulsifiers may combine anionic with cationic character or nonionic with either anionic or cationic activity; *p*H of the aqueous phase makes one or the other function predominant.

Anionic emulsifiers are exemplified by soaps, which can exist only in an alkaline vehicle, or by long chain acidic derivatives active over a wide *p*H

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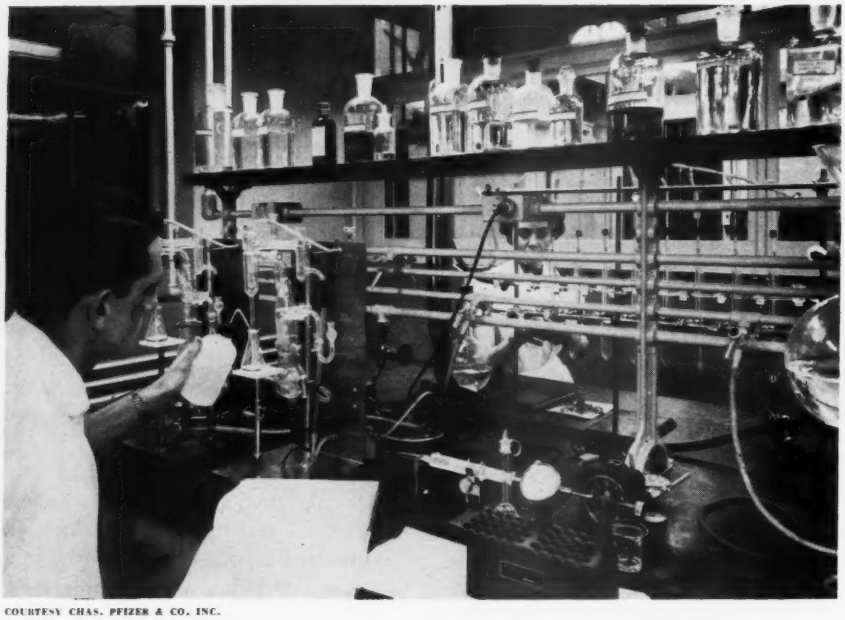

COURTESY CHAS. PFIZER & CO. INC.

DIURETICS AND EDEMA

BY BERNARD IDSON, PH.D. RESEARCH DIRECTOR, JULIUS SCHMID, INC.

The mercurial diuretics are the most powerful diuretics now available, followed very closely by the chlorothiazides and less closely by the carbonic anhydrase inhibitors. All others are usually reserved for enhancing mercurial action or attempting to restore responsiveness to mercurials. The hydrochlorothiazides may be as potent orally as the parenteral mercurials.

Mercurial Diuretics

It has been assumed for years that the diuretic effects of the organomercurials are superior to those of the inorganic salts. This is not correct. The only advantage of the organic mercurials is that they are in general less toxic than the inorganic compounds, regardless of the route of administration. The toxicity of many organic mercurials can be still further reduced by combining them with agents such as aminophylline, theophylline, glutathione, and cysteine hydrochloride. The inclusion of these compounds achieves a potentiation of action and because of increased solubility there is a decrease in local irritation at the site of injection.

With the exception of mercaptomerin sodium, practically all the mercurial compounds are coupled with a molecule of theophylline.

The official mercurial diuretics, recognized in the U.S.P. are mersalyl, (Salyrgan), the sodium salt of mersalyl with a molecular equivalent of theophylline (Mercurophylline), meralluride (Mercuhydrin; methoxymercurisopropyl-succinyl urea) and mercaptomerin thiomerin; [N(γ - carboxymethyl - mercaptomercuri - β - methoxy) propyl camphoramic acid]. Structurally, mercaptomerin differs from Mercurophylline by the replacement of the theophylline molecule by the monothiol, sodium thioglycolate.

Each of the mercurial diuretics contains a divalent mercury atom attached to carbon. The mercury atom is combined also with a hydroxyl group. The mercury is inappreciably ionized, and hence, although it serves as a tubule irritant in effective concentrations, it is not a tubule poison as is mercuric chloride.

Other clinically useful mercurial diuretics are chloromedrin (Neohydrin, 3-chloromercuri-2-methoxy-propyl urea). Neohydrin has taken its place among the most popular mercurial diuretics and offers the striking advantage of a higher degree of therapeutic effectiveness upon oral administration. A somewhat newer mercurial diuretic is merethoxylline procaine, (Dicurin Procaine), procain 2-[N-3′-hydroxymercuri-2′-methoxyethoxy)-propylcarbamyl] phenoxyacetate with theophylline. Clinical reports on

this injectable are, in the main, good. It appears to be effective, well tolerated, with minimal tissue irritation at the site of injection. Mercumatilin (Cumertilin), 8-(2′-methoxy-3′-hydroxy-mercuripropyl)-coumarin-2-carboxylic acid plus theophylline) elicits about the same response as the previously mentioned ones.

The mercurial diuretics have been administered by several routes, but until recently the most common route has been intramuscularly. Here absorption is very rapid. Nearly 84 per cent of the mercury administered is absorbed within the first 24 hours after the injection. The combination with theophylline enhances the absorption so that 95 per cent of the administered dose may be absorbed during the first hour after the injection. A disturbing factor in intramuscular administration is the local tissue reaction at the site of injection.

The reactions vary in intensity from one product to the other. The intravenous route is the most efficient and rapid, but least safe. The oral method was very popular, with Neohydrin (Lakeside) being the generally used and most efficacious. Neohydrin had in many cases completely replaced parenteral therapy and in others served as a useful adjunct to it. However, the intramuscular route produces a much greater diuresis. The newer hydrochlorothiazides have practically completely displaced the oral mercurials.

Various hypotheses were advanced in the past to explain the site and mode of action of mercurial diuretics. However, it is generally accepted that the mercurial diuretics exert their effect by reducing tubular resorbtion of water, by virtue of the action of the organomercuric complex, $R\text{-}Hg^{+}$, with no concomitant tubular damage. Mercurial diuresis produces a marked increase in chloride excretion in the urine. There is a powerful action in the depletion of the tissue salt content, total plasma base and plasma bicarbonate. The increased urinary chloride excretion is accompanied by increased amounts of sodium.

Some of the toxic effects of these diuretics are attributable to the depletion of these tissue ionic constituents.

Available evidence indicates that the mercurial diuretics penetrate tissue cells readily. The compounds appear to be absorbed by cell constituents in the vicinity of the active enzyme systems and produce their inhibition by slowly making available mercuric ions. The sulfhydryl enzymes appear to be principally involved. Mercurials may be powerful and specific inhibitors of the succinic dehydrogenase system *in vivo* in animals. At present it is undecided whether blocking of this succinic dehydrogenase system by mercurials prevents reabsorption predominantly of sodium or chloride. At any rate there is simultaneously obligatory water loss. Mercaptomerin acts by inhibiting succinic dehydrogenase in the distal part of the renal tubule. It prevents the reabsorption of sodium and chloride, and causes excretion of sodium, chloride and water. There is no significant potassium loss, and bicarbonate excretion is temporarily suppressed. The onset and duration of action are approximately the same as those of chlorothiazide. However, it has the disadvantage that it must be given by injection.

The mercurials have been challenged by the newer hydrochlorothiazides. but they are still considered the most effective diuretics and will probably never be completely replaced. Their most serious drawbacks are toxicity, poor oral absorption and loss of activity after prolonged use.

Carbonic Anhydrase Inhibitors

The introduction of the carbonic anhydrase group of diuretics in 1949 was a milestone in this field. During the era of sulfanilamide therapy, several investigators noted that the drug produced acidosis, loss of fixed base from the body and alkaline urine. These observations stimulated a series of investigations which culminated with the discovery that these metabolic effects of sulfanilamide were due to the inhibition of the enzyme carbonic anhydrase in the kidneys. Carbonic anhydrase catalyzes the conversion of carbon dioxide and water to carbonic acid in the renal tubular cells. The breakdown of carbonic acid produces hydrogen ions which are then available for the replacement of sodium ions in the tubular urine and also for the manufacture of ammonium ions.

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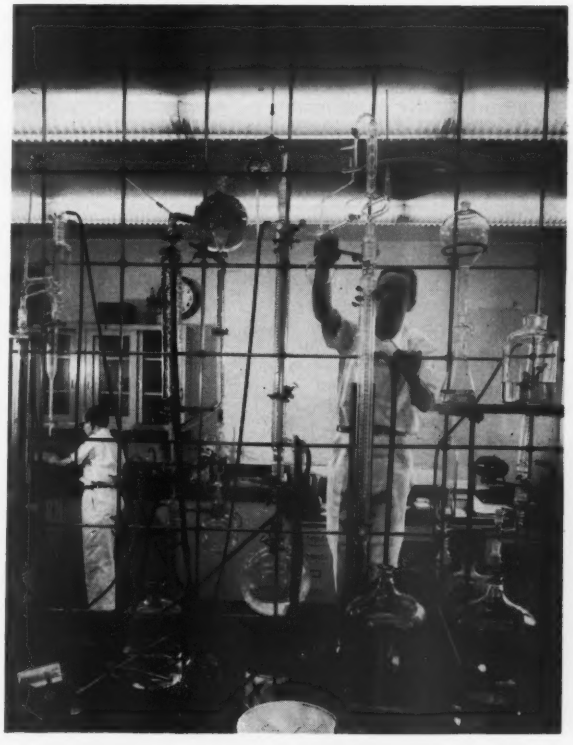
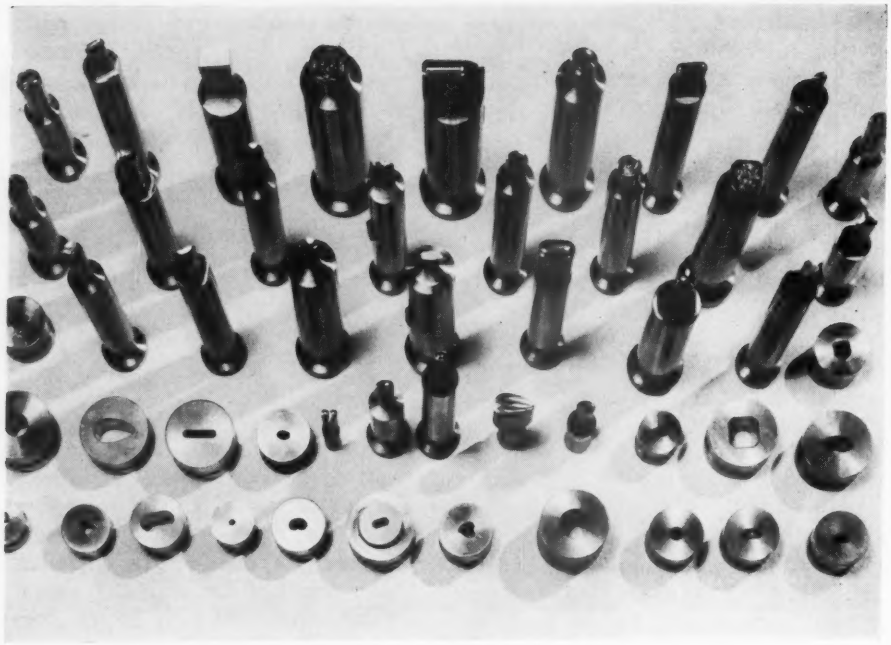
COURTESY EATON LABORATORIES





BUYING PUNCHES AND DIES

BY WILLIAM C. BOBBITT F. J. STOKES CORPORATION

The responsibility for buying tools for tabletting machines varies from company to company and from industry to industry. In some firms and some industries, the engineering department will design each set of tools completely and in detail. Here, the function of the purchasing department is merely to find the most economical and reliable source of supply, which can give the promptest delivery. In other companies and other industries, however, the engineering department will supply only the general configuration and the critical dimensions. Here, the tool buyer will have considerable latitude for the exercise of his judgment.

This article presents some of the basic considerations in buying tools for tablet manufacturing—information which will be of practical use to purchasing executives who may not have had extensive experience in tablet making.

Punches and dies are an extremely important part of the tablet-manufacturing operation. With the *right* tools, modern high-speed presses can deliver all of the precision performance and large-volume output that has been engineered into them. With *poor* tools, some of this capacity may be lost—in idle time caused by shut-downs for tool replacement, in high reject rates of imperfect tablets and so on.

In general, tooling must be designed for the longest possible runs of perfect tablets, which means that quality and workmanship must be of the highest order.

Selection of the proper material for resistance to wear and resistance to fracture is perhaps the most important consideration. Finish requirements, clearances and fits, and proper provision for scrape-off or

A press-coating machine, Stokes Model 538, at Wm. S. Merrell Company, dry-coats 200,000 tablets a day of Bassinate, a vitamin supplement.

relief are also significant factors. Each of these will be discussed in turn.

Selection of Material

Unfortunately, the wear-resistance of tool steels is inversely proportional to their toughness. As the wearing qualities of punch and die materials improve, their resistance to fracture is reduced, and vice versa.

Selection of the type of steel which will be best suited to any given punch and die requirement is normally governed by four factors: (1) the quantity of tablets to be produced; (2) the abrasiveness of the material; (3) punch face characteristics; and (4) pressure requirements for good compacting.

Both high production requirements and highly abrasive materials—whether they occur separately or in combination—make it desirable to use steels with maximum wear-resisting qualities. Such steels are more expensive than those with moderate wear resistance. Hence, when production requirements are not large and when the material is not highly abrasive, economy dictates the use of steels with average wearing qualitites and average toughness.

If the punch faces have sharp edges that are liable to fracture, toughness becomes the paramount consideration and wear resistance may have to be sacrificed. And even where sharp edges are not involved, when the pressure requirements are very high and/or when the tablet diameter or size is small, extreme toughness may be required to prevent fracture.

In making the final selection of the proper punch and die material, the maximum safe pressure which it can be used to exert is often the controlling factor. The amount of compacting pressure required for a tablet of a certain diameter or area, with a particular surface contour, made from a specific material, will be dictated by the production department—based on research or previous experience. Starting with this factor, tabulations such as those shown in Table 1 can then be used for selection.

TABLE 1
Maximum Safe Pressure in Tons on Tablet Machine Punches
(Made of Stokes Standard No. 3 Punch Steel)

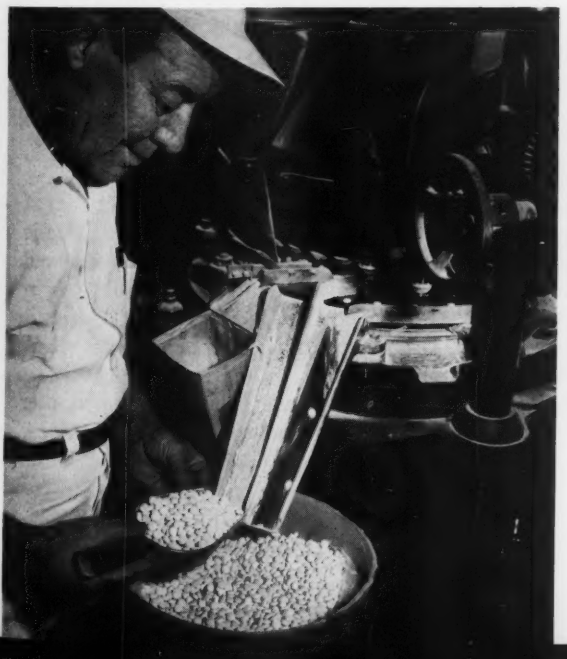
Punch diameter (inches)		Area of punch face (square inches)	Type of Punch Face	
Fraction	Decimal		Flatface of standard concave (tons)	Bevel-edge, modified ball (tons)
1/8	.1250	.0123	0.6	0.24
5/32	.1563	.0191	1.0	0.40
3/16	.1875	.0276	1.4	0.6
7/32	.2188	.0377	1.9	0.8
1/4	.2500	.0491	2.5	1.0
9/32	.2813	.0620	3.2	1.3
5/16	.3125	.0767	3.9	1.6
11/32	.3438	.0929	4.7	1.9
3/8	.3750	.1105	5.6	2.2
13/32	.4063	.1295	6.6	2.6
7/16	.4375	.1506	7.7	3.1
15/32	.4688	.1726	8.8	3.5
1/2	.5000	.1963	10.0	4.0
9/16	.5625	.2485	12.8	5.2
5/8	.6250	.3068	15.3	6.4
11/16	.6875	.3712	18.6	7.4
3/4	.7500	.4418	22.1	8.8
13/16	.8125	.5185	25.9	10.4
7/8	.8750	.6013	30.1	12.0
15/16	.9375	.6910	35.5	14.0

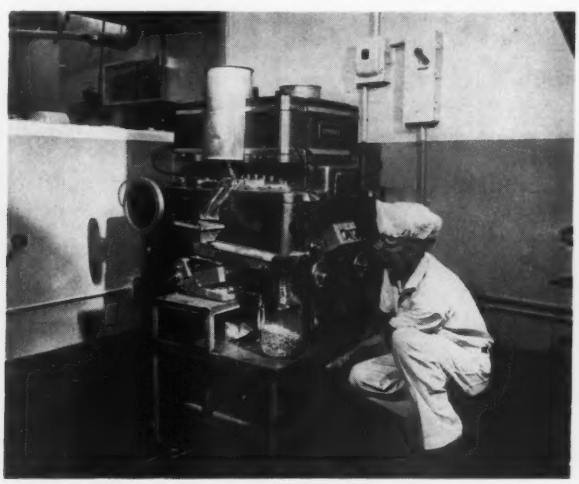
Table 1 gives the maximum safe pressure in tons for various sizes and shapes of punches made of Stokes Standard No. 3 punch steel. No. 3 is a low-cost, fairly tough steel, suitable for moderately high production quantities. It is the material from which about 80 per cent of the punches and dies made by the company for its customers are fabricated. Similar tables are available for each of the other types of punch material in common use. The ability to draw on information such as this is just one advantage which the tool buyer can gain from close consultation with experienced tooling suppliers.

Here is how the tool buyer can make use of such tables:

Example 1. Assume the need is for a one-quarter inch tablet with standard concave face requiring

Two-layer tabletting machine, Stokes Model 563, at Pharmaceuticals, Inc., which compacts Somines tablets, and runs as much as 16 hours a day.





A Stokes Model 540 rotary tabletting machine turns out Terramycin tablets of 1500 to 1800 per minute at Chas. Pfizer & Company, Inc.

Closeup of the Stokes rotary tabletting machine at Chas. Pfizer & Company, which can make as many as 1800 Terramycin tablets per minute.

three tons of compacting pressure.

From the entry on Table 1, line 5, we see that the maximum safe compacting pressure to be exerted on a punch made of No. 3 steel is 2.5 tons. This is less than the required pressure, and hence such a punch cannot safely be used.

There are three options open:

(1) Improve the granulation so that the required compacting pressure is only 2.5 tons. Then it is safe to use this low-cost steel.

(2) Increase the diameter of the punch to 9/32 in., the next larger diameter. Permissive pressure is now raised to 3.2 tons, making it safe to use No. 3 steel (This means modifying the dimensions of the tablet if the weight of the tablet must remain constant.)

(3) Make use of a tougher steel than No. 3, to obtain a punch having greater pressure-resisting strength.

Example 2. Assume the need is for a one-quarter inch tablet of a modified ball shape, that is, a contour which calls for a punch having a deeper concavity and hence results in a thin-edged punch tip. Again line 5 of Table 1 indicates that the maximum safe pressure that can be exerted with this shape of punch made of No. 3 steel is one ton. If the required compacting pressure for the material in question is more than one ton, a punch of No. 3 steel cannot safely be used.

The same three options are then available, plus a fourth:

(4) Reduce the depth of concavity and thus reduce the thinness of the edges to a point where the maximum safe pressure is equal to or greater than the required compacting pressure.

From this tabulation (and similar ones), it is apparent what an extensive effect the depth of concavity of a tablet surface has on punch and die materials.

In making the selection of the most suitable material for his punches and dies, a purchaser is well advised to seek the advice of an experienced source of supply. Firms with an extensive background in tablet manufacturing have the practical knowledge for recommending the best choice in the customer's specific situation.

Moreover, Stokes, for one, is constantly conducting in-service tests of new steel formulations. For example, an experimental set of punches and dies for a B2 16-station rotary tabletting press—with half of the dies made of Stokes Standard No. 2 steel and the other half made of a new and still experimental different type of steel (the punches all being made of one type of steel)—was supplied in May, 1958, to Richlyn Laboratories, Philadelphia, to determine the comparative wearing qualities of the two different types of die steel under actual tablet-making conditions. A year later, in May of 1959, production records showed that a total of 68,000,000 tablets of thyroid, digitalis and other granulations had been produced from this set. So far, practically no wear is apparent in any of the stations, and the dies have not yet been reversed in the table. The test will be continued until all stations are worn to a point where they must be replaced. At that time, we will have an exact record of the total number of tablets produced from each set of punches and dies and therefore will be able to evaluate the comparative wearing qualities of the two different kinds of steels. This is just one of the tests we are constantly making in an effort to provide punches and dies of the highest quality.

From our experience in selecting suitable steels for specific punch and die applications, we have developed a number of special steel formulations with which we regularly work. Table 2 (See page 542.) lists the properties and characteristics of these steels and an index of relative costs, as well as our general recommendations for their use in punches, punch tips, punch inserts, holders, core rods, and dies.

Holders and Inserts

If it is necessary to purchase tools for the same job with a high degree of frequency, a tool buyer would be well advised to investigate the possibility of reduced tool costs by the use of holders and inserts instead of solid punches. If he is presently using *solid* punches and dies, and if the full range of steels (including carbide) has already been investigated, there is a possibility that economies may be obtained

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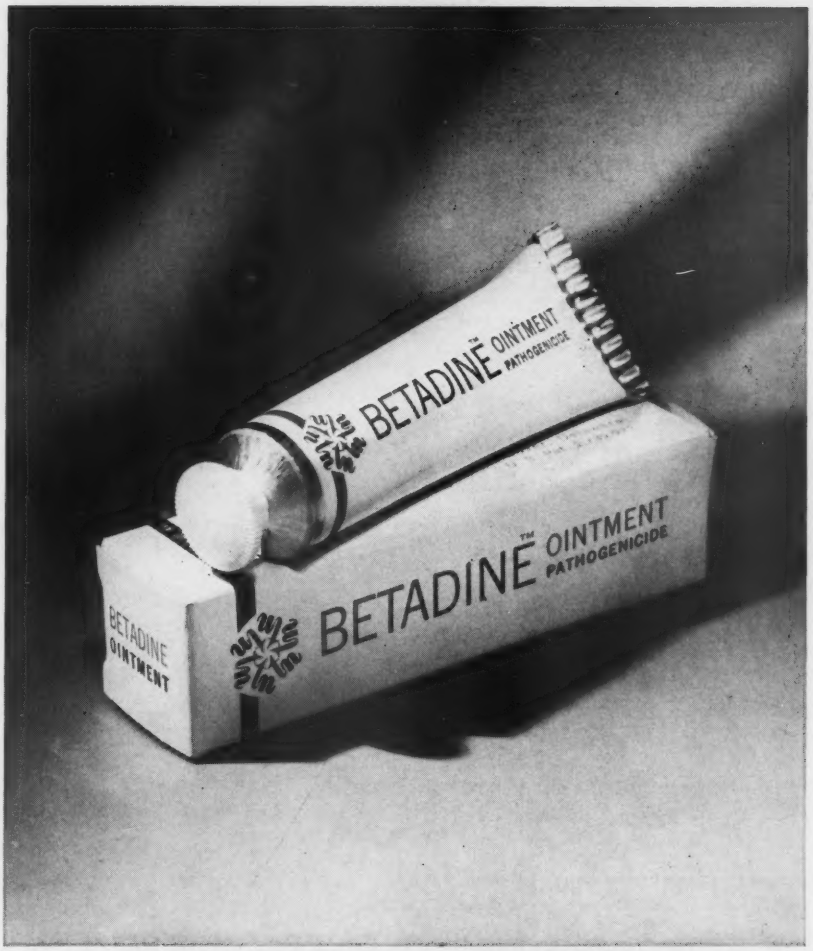
Packaging and Selling



New topical ointment for control
of skin and wound infections, Betadine, by Tailby-Nason Company, in a collapsible tube. Lettering on the carton, as well as on the outside of the tube, is in blue and brown, the band is brown. Povidone-iodine, the active ingredient, is nonirritating, nontoxic, and nonstaining.

℞ *Protection*

The protection of family health is the single goal of America's giant pharmaceutical industry. Its thousands of modern formulae demand the finest in protective packaging. Sheffield collapsible metal tubes are the choice of leading manufacturers; their quality, safety, utility are without equal.

THE SHEFFIELD TUBE CORPORATION

Home Offices:

New London, Connecticut

Sales Offices: New York

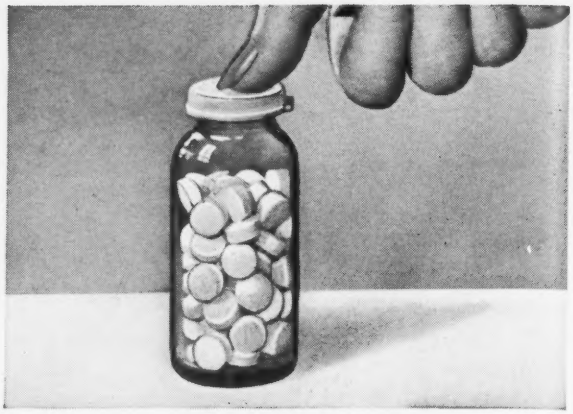
Chicago, Los Angeles

FAVORED IN THE PACKAGING OF PHARMACEUTICALS

In cosmetics, industrial and household product packaging, also!

SHEFFIELD TUBES

Off with ease



... closed tight quickly

The new Safety Cap keeps medications safe from children's hands . . . yet adults remove it easily

Owens-Illinois Snap-Caps
provide a perfect seal for dry products

Owens-Illinois plastic Snap-Caps offer use-convenience and tight, durable protection for dry products at all times. Off and on with a flick of the fingers, these tight-sealing closures stay clean and secure, no matter how many times they are handled.

The Safety Cap is another development from Owens-Illinois. It offers the advantages of Snap-Caps in ease of operation, yet it is difficult for little children to remove . . . keeps medications away from inquisitive hands. For complete information about Snap-Caps as the ideal closure for your package, call your nearest O-I office, or write to Owens-Illinois, Toledo 1, Ohio.

PRESSED PLASTICS
AN (I) PRODUCT

OWENS-ILLINOIS
GENERAL OFFICES · TOLEDO 1, OHIO

SIMPLIFIED PACKAGE SELECTION

BY GEORGE M. SCATTERGOOD ARMSTRONG CORK COMPANY

COURTESY GLASS CONTAINER MANUFACTURERS INSTITUTE

The long standing tradition that popular or heavy-volume dry prescription products must be packaged in set quantities ranging from 100's to 1,000's has resulted in hundreds of different-sized packages presenting many problems to both the pharmaceutical manufacturer and the pharmacist.

A simple solution to this problem would be to adopt a median package of the capacity most often used. This package might hold 425 units of one size product, 500 of another size, or 1200 of another size, but the package would remain the same size. Only tradition says that a certain number of tablets or capsules should go in a package. Instead of changing the package size for different quantities, why not change the quantities?

With the development of new prescription products at the rate of nine a week, there has been a move toward controlled dosage for better measurement by the user. Eighty per cent of present prescription items did not exist ten years ago. Manufacturers are copywriting shapes and colors for product identification and to protect against counterfeiting. Some tablets have become trademarks; others have been granted design patents. As these new items become popular they are sold in large quantities, from consumer sizes to quantities of 250 to 500, 1,000 to 5,000, and even 10,000.

The various shapes and sizes of these products make it necessary to have many different bottles, as many as 50 different-sized containers for 1,000 quantities alone. One manufacturer has as many as 1,400 different packages.

The majority of prescriptions are written for pharmaceutical specialties by trade name, and specified by name of manufacturer. Few, if any, of these specialties are truly competitive. Even if two products are offered under the same therapeutic indication category, price comparisons at the point of sale in most retail outlets are rare. Specialties are not compared in price like aspirin or Epsom salts or U. S. P. or N. F. products. Neither are they compared in price by consumers like proprietary remedies, which are advertised, and for which size, value, and price all have frequent competitive comparisons.

Thus there is little reason to have many different-sized packages merely for the sake of comparison. These hundreds of different packages must be ordered individually in quantitites related to the movement of the specialties. Most are labeled with labels of different sizes. If individual cartons are used, each has a different-sized carton.

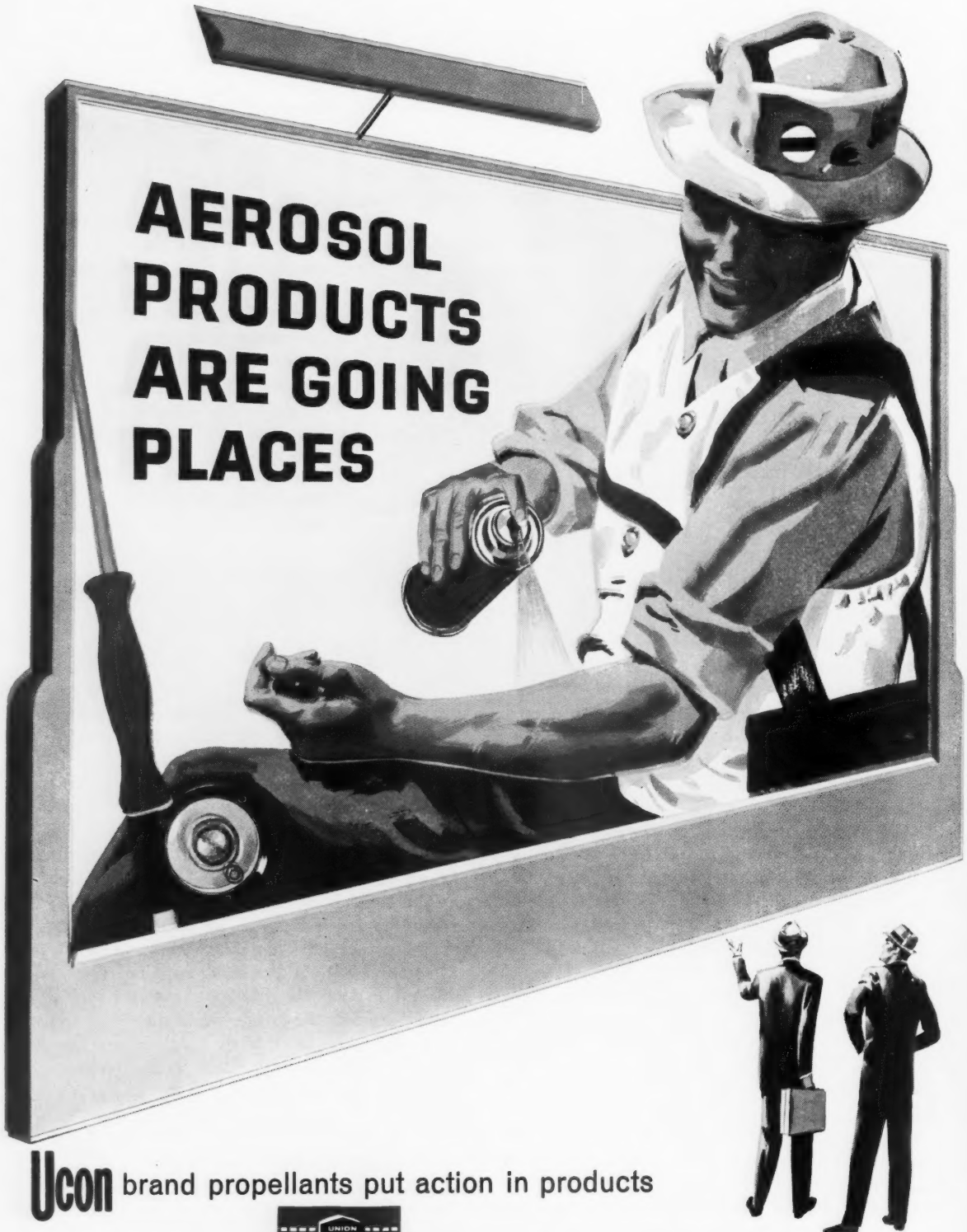
Warehouse space must be provided for hundreds of different stockpiles. The buyer's problems are many times multiplied. Procurement difficulties often include delays for short runs, price penalties for less than minimum runs, and added transportation expenses. Hundreds of sizes of containers include excesses not only in sizes and types of closures but also in shipping containers.

Another problem is the filling line. Numerous filling machine changes are needed for varying heights and body dimensions of containers. Also, when the specialties are packed for shipment, the shipping cases have as many sizes as there are package sizes. Multiple dozens of shipping case sizes are difficult to load for shipment, even in carload lots. Stocks are difficult to pile when dimensions of cases vary, bringing hazards of toppling and breakage, and making palletizing relatively impractical.

When the products reach the pharmacy shelf, orderly arrangement of the varying sizes separates the manufacturer's line, or a mixture of size and shape makes orderliness impossible.

Some manufacturers temper their range of package sizes with the use of varying quantities of cotton or cotton-like material. This saves a part of the bur-

(*Continued on page 556*)



Ucon brand propellants put action in products

UNION CARBIDE
Ucon
BRAND
propellants

Why don't you discover Ucon Propellant service, too?

UNION CARBIDE CHEMICALS COMPANY
Division of Union Carbide Corporation
30 East 42nd Street, New York 17, N. Y.

Ucon and Union Carbide are registered trade marks of Union Carbide Corporation

From September tenth through November ninth, the Museum of Modern Art in New York City is presenting an exhibit called, simply, The Package. The almost 300 containers range from a 24-foot collapsible black rubber tank with a capacity of 20 tons of liquid, through a seed-ribbon of water-soluble methyl-cellulose film.

The show is under the direction of Mildred Constantine, associate curator. Wilder Green, assistant director of the department of architecture and design, installed the exhibit, which was co-sponsored by the Container Corporation of America, the Reynolds Metal Company, and the National Distillers and Chemical Corporation of America.

Following is the Museum's introduction to the package show, and a list of the packages of interest to the drug and cosmetic industry which are not pictured here and on page 479.

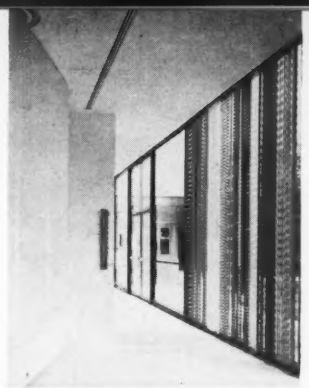
PACKAGING
An Applied Art

The Museum has devoted many exhibitions to such well-designed useful objects as furniture, household equipment, and automobiles. This exhibition is concerned with another kind of artifact no less prominent in our daily lives but seldom considered for its aesthetic quality: the package.

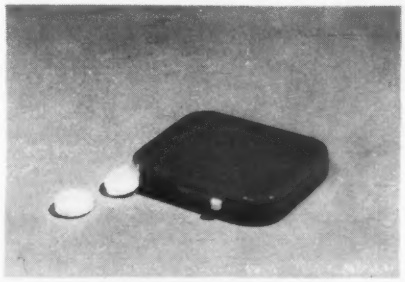
"Webster's dictionary defines a package as 'a bundle made up for transportation; that in which anything is packed; a box, case, barrel, crate; a container.' Well-designed packages protect and preserve the things they contain, sometimes facilitate their use, and are often beautiful objects in themselves.

"The exhibition is not concerned with what is called motivational research, merchandising, production costs, or the merits of the product inside the package. Its purpose is to appraise packages of all sorts for their design qualities, and in so doing to reexamine and perhaps broaden our ideas of what actually does constitute a package. To do this, packages have been removed from their conventional context of advertising and sales. Printed words and images have been included only when they make an important contribution to the total design. The packages on view have been selected for excellence of structure and shape, color, texture, proportion, and the suitability of these qualities to functional performance.

"Packages may be grouped conveniently within two major categories:

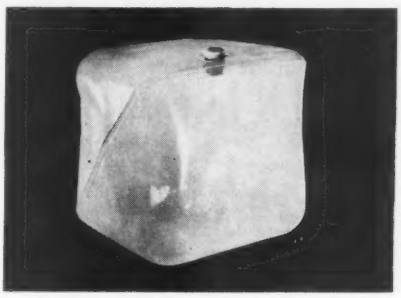


Green, white, red, blue, clear pillow packs, Enko Creations, Inc.; and purple unit-dose saran dispensers, Unette Corp., designer, F. E. Brown.



Plastic aspirin dispenser, Squibb, by W. Christiansen, N. Waterman.

Glass bottle for Sucaryl, Abbott Labs., by Raymond Lowey Associates.



Polyethylene Cubitainer with plug, Hedwin Corp., by T. W. Winstead.

Plastic squeeze atomizer, Norwich Pharmacal Co., by Eaton Laboratories.

Aerosol packaging captured 67% of the $47,000,000 room-deodorant market

If your product can be brushed, poured, sprayed or squeezed, this profitable new packaging idea can generate sales for you, too!

A runaway in room-deodorant sales started in 1953 after the aerosol-packaged product was introduced. By 1957 total sales were up to $47,000,000, and the aerosol form accounted for $31,500,000 of this.

The reasons for this success are simple. Aerosols deliver the product in a completely new form that's easier, more effective and often more economical to use. If your product can be brushed, poured, sprayed or squeezed, you stand a good chance to add new sales appeal—create vast new markets—if you package it in an aerosol.

It is not necessary to set up your own packaging line to enter this field. A custom filler near you has the knowledge and equipment to help in every area, from planning through production.

If you don't know the name of a custom filler, write Du Pont. We'll send you a list and include survey data on your market for aerosol products, plus information about Freon* propellents for aerosols. "Freon" is preferred by custom fillers and is used in more of today's aerosols than any other propellent. Write E. I. du Pont de Nemours & Co. (Inc.), "Freon" Products Division 3410, Wilmington 98, Delaware.

Best-selling aerosols are powered with

FREON®

PROPELLENTS

DU PONT

REG. U.S. PAT. OFF.

BETTER THINGS FOR BETTER LIVING ... *THROUGH CHEMISTRY*

*Freon and combinations of Freon- or F- with numerals are Du Pont's registered trademarks for its fluorinated hydrocarbon propellents

Disposable plastic veterinarian's syringe for Metibiotic, Schering Corp.

"THE DISPOSABLE PACKAGE, intended to be thrown away after one use, such as wrapping paper, toothpaste tubes, cans, and plastic squeeze bottles. Disposable packages are those most often seen and used by the public.

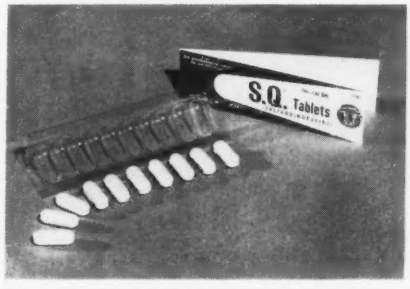
"THE RE-USABLE PACKAGE, intended to have continuing use for its original purpose, such as barrels, drums, and other bulk containers. Most re-usable packages are designed for industry and are seldom seen by the public. On the other hand, a leather suitcase, a jewel box, and a shoe-shine kit are re-usable packages with which everyone is familiar . . . .

"In this exhibition the packages are for 'objects' ranging in size and weight from tiny seeds to twenty tons of milk. They vary in complexity from multipurpose primitive baskets to such highly specialized working packages as a disposable paper house and a plastic bag tailored to contain a man.

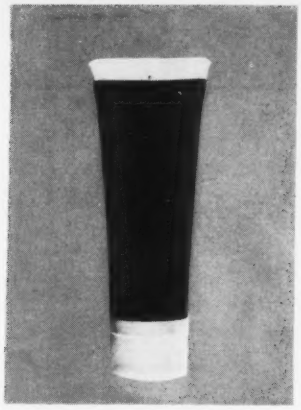
"An alarming number of packages are more elaborate and more costly than the things they contain. Some packages are altogether wasteful. The exasperated victim of such proliferation struggles each year with tons of wrapping, and with 'miracle' seals or closures impossible to open without special tools and adequate information. But the attention now devoted to package design recognizes that our artifacts have become so numerous and often so complicated, that their usefulness is largely determined by problems of transportation, storage, and protection.

"The package designer may be a technician with special knowledge of materials or he may be the designer of the product. He may also be called upon to design the machines that will make the package. Thus in designing useful objects he must increasingly take into consideration the manner in which they

(*Continued on page 572*)



Plastic mold holder for veterinarian S.Q. boluses, Merck and Company.

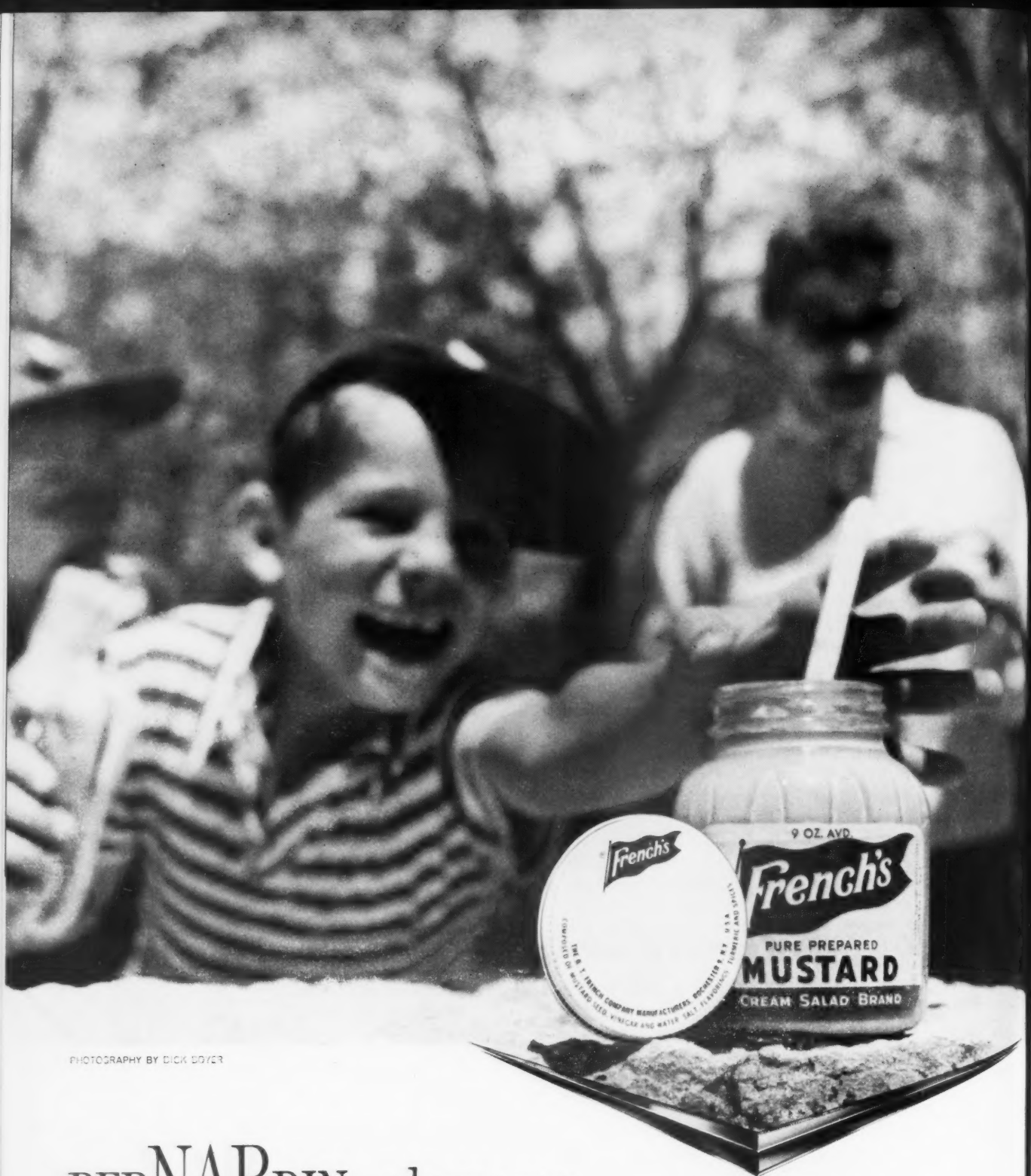


Plastic tube, stand-up cap, Noxzema Chemical Co., by C. H. Magers.

Plastic roll-on dispenser, Imco Container Corporation, company design.

Aluminum bottle for toilet water, Carmel Myers, Inc., by Fragonard.

Polyethylene container for acids, Pirelli, Milan, by Roberto Menghi.



PHOTOGRAPHY BY DICK BOYER

BERNARDIN closures keep good company!

Brand Preference is the expression of customer satisfaction earned by a product over its competitors. We like to feel that our relations with "French's Mustard" likewise confirms the expression of the several satisfactions a closure must provide "on the line," during shipping, at the retailers and in the consumer's hand. *May our Closure Craftsmen work with you?*

SINCE 1881 · BERNARDIN BOTTLE CAP COMPANY, INC., EVANSVILLE, INDIANA

Packaging and Selling

Big shelf space may not necessarily mean increased sales.

What a bomb explosion this would mean in the sales department, and yet, some preliminary tests over a period of six weeks in a group of six supermarkets, seem to indicate this.

We are drawing our conclusions from an article in the trade magazine, *Super Market Merchandising*, by Mack Hanan, a marketing consultant who conducted the tests.

In these tests special shelf displays were set up for two different brands of detergent. Both were all-purpose cleansers heavily advertised in similar media, competitively priced and packaged, and dependent on a comparable selling point. At the time of the test both were being sold without benefit of incentive devices such as premiums, two-for-ones, or other price deals.

Within each of the six supermarkets three different shelf-facing lengths were rotated over the six-week test period. This meant that each of the brands had equal time in each of the shelf lengths.

Here are the startling conclusions. To quote, "No matter when or where the display length of either one or the other brand was increased, the number of brand selections for both remained relatively unchanged compared against average case sales for the six weeks previous to the test. Whether one brand outdisplayed the other, or whether both brands shared adjoining displays of equal length, sales remained approximately the same."

Mr. Hanan ventured some conjectures.

(1) Pressure for more and more shelf facings per brand may not always help sales, for some of the brands at least. How many facings of each brand provide the best sales incentive for that particular brand?

(2) Pre-selling by means of massive advertising saturation may have made the display of some products "unstimulating." It makes the display unable to change significantly a pre-sold intention to buy something else. Is it possible that the more heavily a product is advertised, the more lightly a display is taken?

(3) If length of shelf facings is not the most critical display factor in moving some supermarket products, what is? Would smaller "spot" displays, displays in surprise locations, related-item displays be more influential? Or, are permanent premium or other price inducements more important than either the product itself, its number or arrangement on the shelves, or its location in the store?

However conclusive this limited test may be, at the very least, it gives rise to some provocative questions.

The magazine *Beauty Fashion* has just completed a survey among department and drugstore personnel.

This may not be the first time that a company image survey has been made within the trade rather than among consumers, but at least it is the first time we have heard of a trade-image survey.

We seem to be in a period where a great deal of interest is being generated both in the retail trade for store images and among manufacturers for consumer images of their companies.

According to a few of the consumer image studies which we have seen for cosmetic companies, there can be a shocking variation between the rosy opinion that a manufacturer may have of his products or policies and the opinion that the public holds for these two same things.

As *Beauty Fashion* discovered in its survey covering 19 perfume and cosmetic companies, just about the same condition applies.

For this survey, a broad list of questions were asked of executives and sales people in department and drugstores, questions which sought to determine the trade's opinion of each company regarding its position as a fashion leader or a mass consumer leader, its pricing and promotion policies, its packaging, the effectiveness of its advertising and the general character of its distribution. The two final questions, which unexpectedly brought a large volume of comments, were, "Do you admire the company?" and, "Do you like its products?"

Full details of this survey are being published in the September and October issues of *Beauty Fashion*. The 19 companies are not mentioned by name, but a fairly close description of each one places the company in a specific classification and gives a pretty good chance for anyone intimately connected with the industry to guess at the name.

Among these 19 companies, two treatment houses and two perfume companies came up with a superb degree of trade approval and trade accuracy in pinpointing their policy.

Several of the other companies had such blurred personalities in the eyes of the trade as to make it abundantly clear that they are working under substantial handicaps in every phase of their selling and advertising.

One company specifically was pinpointed with accuracy but loudly labeled with disapproval.

Here's what variety stores find is needed in packaging for self-service. The merchandise must sell itself (1) by its attractive appearance—and this means that in most cases merchandise must be seen through

some transparent material or look-through packaging device; (2) by being protected from customer handling, sunlight, dust, and other factors; (3) in the case of small items by possessing so-called pilferproof boxes and cards, so that they cannot be easily slipped into pockets and purses; and (4) by packaging conveniences (eyelets, hooks, etc., for hanging on convenient racks) for optimum display, and the boxing and packaging of unusual and irregular shapes and sizes in a uniform manner for easy shelf stacking or bin storage.

The 23rd Annual Variety Packaging Awards Competition sponsored by Variety Store Merchandiser is now taking place. There are 974 entries in the competition this year, an increase of approximately 300 over last year.

An interesting feature of this competition is the new division just started to give recognition to the packages of private-label merchandise carried under a chain store's own name. Among the important leading chains who entered their private-label packages in the competition were Woolworth, Kresge, Kress, Grant, Neissner, Newberry, H. L. Green, Butler Brothers, Sears, Montgomery Ward, and McCrory's.

Five major packaging factors are used as a basis for judging packaging in the competition: (1) display value, (2) sales information, (3) merchandiser protection, (4) consideration of retailer problems (shelf or counter room, stacking, etc.), and (5) package economy.

The man who has the last word about a $96-million advertising budget, that is, Charles G. Mortimer, president of General Foods, said some highly interesting things at the last annual meeting of the corporation.

For instance, this most quotable sentence: "The surest way to overspend on advertising is not to spend enough to do a job properly. It's like buying a ticket three-quarters of the way to Europe. You have spent some money, but do not arrive."

Here are some more quotes: "When we start to make up our market plans for the year, we do not say, 'We will spend so-and-so-much for advertising.' Rather, we ask ourselves, as the plan is made for the promotion of an individual product, 'What will it take in advertising and sales-stimulating inducements, first, to maintain the market position of this particular product (if it is already an established product) and, second, to increase the volume of its sales, if we believe that to be possible?'

"If it is a relatively new product, such as Tang, for example, we may ask ourselves, 'How fast is it feasible to try to build volume for this new product, and what will such a rate of growth call for now in advertising and other forms of sales stimulation?'

"Usually these calculations result in an appropriation based on so many cents a case, applied to the early sales of the product, and also to the forecast of case sales we believe it will be possible to add."

Does advertising pay? According to Mr. Mortimer, "It has to or we could not continue to pay dividends to stockholders, nor increase the volume of present products and introduce new products to provide better profits and dividends in future years. Yet, I believe we do get our advertising expenditures back—and with a profit."

Just how does advertising pay? It pays, says Mr. Mortimer, "by developing such a large and dependable volume of sales that we can keep our plants running at high efficiency in terms of processes and machine operations. And I hardly need to remind you of the importance of this, steadily increasing costs being what they are.

1. "We can utilize the special skills and the time and energy of our people to full advantage.

2. "We can turn our inventories and raw materials rapidly, and hence keep our working capital turning swiftly and profitably.

3. "We can protect the future value of our stock by maintaining a sound rate of company growth."

This month we were privileged to examine a bath and shower aid which has just arrived from West Germany. We have not yet had time to do any clinical work in a bathtub on this product but are looking forward to it with keen expectation.

The reason is that the product, called "Vita-Bath," contains five vitamins, A, B_3, E, F, H, also chlorophyll and ultra-mild soapless cleansing agents.

While you are in the bathtub, Vita-Bath relaxes, refreshes, cleanses, deodorizes; it does not leave a bathtub ring, but will leave the skin smooth and fragrant.

According to a statement by Ernest H. Volwiler, chairman of the board of Abbott Laboratories International, in a recent commencement address at the Chicago Professional Colleges of the University of Illinois, "The scope of research activity today in the pharmaceutical industry is not generally understood by the public." We would guess that it is not even well understood within the industry itself, aside from a small circle of leading pharmaceutical companies.

As Mr. Volwiler said, "A recent study by the Pharmaceutical Manufacturers Association disclosed that the industry in 1958 tested about 115,000 substances. A great many more materials underwent routine preliminary screening for physiological activity. Only 1,900 substances—or about one drug out of 60—reached the clinical testing stage. All of this resulted in the market introduction of from 20 to 30 really new drugs, each representing large effort in research and development. And only a few of these will be real commercial successes."

In other words, what could be called fantastic

wastage is necessary in research to attain a truly useful result or, perhaps we should say, thousands of false starts leading to false conclusions must be made and abandoned before the one great result is attained.

It looks as if, even in the most modern, most efficient, and most brilliant research laboratory, serendipity is far from dead.

According to the head of a big research organization, new product introductions will increase from 10 to 15 per cent this year.

The head of a large manufacturing company recently said, in a speech, that his company's marketing success depended upon a program which made their products "exciting" by a constant change in the introduction of new products, new variations of old products, new packages and repackaging.

Compare this to figures of the U. S. Small Business Administration, which states that 98 per cent of all new products will fail, and add to it the recent *Beauty Fashion* survey, which showed only eight products out of 1,000 had a commercial life of over three years.

Since retail stores do not have rubber walls and available shelf and floor space is pretty well jammed already, successful introduction of most new products must mean that a more or less equal number of old products must go out of existence.

We could well ask, in this age of spending so much for research, why the good products don't live longer, and whether we are not overdoing this thing by displacing a valuable and useful old product simply by adding some gimmick change that will lure consumers but give them no better a product. In other words, is the expense of continually bringing out new products worth it?

A casual survey of some of the most successful manufacturers of the last few years seems to indicate an emphatic yes as the answer.

Just one example, that is Chanel Perfumes, would provide an outstanding case history. For many years this fine company with its superb classical odor, Chanel #5, has continued in a stately way and with a very slow growth until just a few years ago, when it had reached the $3-million annual sales mark.

At this time thinking in Chanel underwent a change and a series of packaging innovations were introduced by the company with an increase in the advertising budget.

People in the trade are well acquainted with the beautiful new packages introduced by Chanel over the last three or four years. The very significant thing here though is that these have been purely package or application ideas and not, in any sense, a change of product. The product is still Chanel #5, still rigidly adhering to its superbly successful original formula.

Nevertheless, the new packages, each of striking originality, has increased Chanel's business over 250 per cent in hardly more than three years.

Some day maybe all the figures in this unusual change of philosophy with its superb business success will be made public. At present, however, the entire industry is conscious of what can be done with a fine old product, simply by applying imagination and ingenuity and in offering the public new and beautiful packaging, new methods of application, and the use of modern packaging materials.

This year has seen an epidemic of "spectaculars" in advertising, partly because of new rulings by the post office, but also out of a frenzy of imitation. Magazine advertisers have used inserts running up to 64 pages in every conceivable size, shape, and method of folding.

Undoubtedly, a primary reason for these enormously expensive spectaculars in multiple-space advertising has been the feelings of many frustrated advertisers regarding the enormous expenditure it takes to secure the reader's attention today, and even more frustrating, the enormous expenditure it takes to retain even a small degree of memory for a product, a brand name or anything they advertise.

Judging from a number of recent comments by so-called advertising experts, it would seem that this imitative spell of lavish expenditures, where by so much money is thrown into one single mammoth impression, is beginning to lose some of its charm. The ancient experience of advertisers, that repetition counts in the long run, seems to be regaining its hold.

It would be wrong to deny that the sepectacular has its place in advertising. For the introduction of a new product with a great potential, or of a new policy that it is very important to establish quickly, or for anything new that holds great promise, a spectacular can usually do a wonderful job, providing it does not gobble up too much of the advertising appropriation. But the spectacular has evidently fallen flat on its face when an advertiser lacks the money to follow up with repetition.

It is needless to point out to anyone with real advertising experience in today's market that to get the public's attention is a constant, never ending fight. It is an even bitterer constant fight to obtain any degree of memory recognition from the public or part of the public.

One authority, in his book on advertising, states, "Few advertisers have explored all the angles of the problem of 'continuity.' Much of the value of advertising is lost unless plans are made to achieve a continuity of psychological impression in the minds of the advertiser's prospects. To have an accumulating awareness, knowledge, or understanding of the product or proposition, they must see the advertiser's message frequently and they must be able to connect up in their minds the parts of the message that they see over a period of time."

The Magic Touch of Aerosol Packaging can give your products "feminine appeal"

If you have a woman's product, and want to gain entry to milady's chamber for it, consider the advantages of aerosol packaging. The convenience. The glamorous new container shapes, colors and textures. And the high state of development of the aerosol "art."

Aerosol packaging has a magic touch in helping to sell products for women. Hair sprays are the largest selling single aerosol product group—115 million units in 1958.* Aerosol colognes and perfumes have proved phenomenal sellers—shooting up from 5.4 million units as recently as 1955 to 28 million units in 1958.* Aerosol hand lotions and creams are showing a similar increase, as are aerosol personal deodorants. If you have a product in any of these fields—or a related one—you should be considering aerosol packaging *right now!*

How General Chemical can help you

General Chemical manufactures the right propellant for every cosmetic aerosol need under its trade name "Genetron." These propellants can give your product exactly the right "push" your aerosol formulation requires.

*Estimated by Market Surveys Department, General Chemical Division, Allied Chemical Corporation.

As a leading supplier of aerosol propellants, we will be glad to help you get started in aerosols. We will supply you with market information and technical data. We can tell you about promising new types of aerosol formulations developed in our laboratories. And we can give you information on how contract fillers can help you, from test marketing right through to full commercial production. The fact is, through the use of contract fillers you can get into aerosols without investing a cent in special equipment or personnel!

Why not take advantage of these General Chemical services *now?* Just call or write.

genetron®
aerosol propellants
Putting the "push" in America's finest aerosols

Allied Chemical

GENERAL CHEMICAL DIVISION
40 Rector Street, New York 6, N. Y.

Another expert in this book writes, "Repetition reinforces and strengthens the impressions made on the audience. Each time an idea is repeated, the impression becomes stronger. Each time an impression is reestablished, it tends to last longer."

This industry has some very successful advertisers who have not only practiced a fixed policy of continual repetition, but a frequent policy of repeating the same advertisement. Chanel, Inc., for instance, uses a basic list of magazines with 12 insertions, and the company is famous for frequent repetition of the same advertisement. Quite a number of case histories can be cited in this trade to show that an unusually good advertisement is remembered by the customer, and his attention is reinforced by repeating this same advertisement, rather than constantly changing each advertisment, even with repetition.

Magazine advertising has no conclusive figures to show how many people will receive an impression from an average advertisement in a magazine during the interval of reading. It is probable, however, and many studies support the conclusion, that a relatively small fraction of the reader audience will receive any impression from a good advertisement in a single reading. However, this good advertisement repeated over a period of several months may well register on the majority of that magazine's reading audience. The most famous example of this is the advertisement of Dana Perfumes, that is, the man with the violin, which has been reproduced many millions of times in a large list of magazines over several years. This theme is still in use.

Another need for repetition in product advertising is, undoubtedly, the continued repeat, featuring the product in each advertisement. This identification in the consumer's mind of the product which they will see on the retailer's shelf has been the primary feature in Chanel advertising and in a wide range of package product advertising. In the recent seminar conducted by McCall's Magazine with a group of chain store executives, this need to display the package prominently on the retailer's shelf was stressed as an element in good marketing for all advertising.

Johnson & Johnson is readying the tenth annual promotion of "Emergencies Don't Wait Week." This has been one of the most profitable promotions in the industry. Last year 43 governors and 850 mayors urged public observance of the week, and a survey conducted by Neilsen showed the participating stores enjoyed a significant sales advantage over non-participating stores.

People who do business with Wallerstein Company must surely have it fixed in their mind that these folks have established themselves at their new home on Staten Island.

The reason for this is an effective mailing piece that went out to 4,500 people in the industry.

This mailing piece, which had a 5 cent piece glued inside a cut out, stated, "Where can you take a 25-minute boat ride across five breeze-clean miles of water for only one nickel?

"The place is New York—the boat is the Staten Island Ferry that plies from the Battery to Saint George. Outward bound from Manhattan, you pass Fort Jay, the Statue of Liberty, freighters and flat-tops and car floats, and—if you are lucky—fireboats spraying, tugs hooting and copters swooping to welcome a gleaming new liner as she completes her first voyage. When the ferry warps into the slip, though, the best part of your day is just beggining."

This means a red carpet treatment and a tour of the new offices and laboratories.

American-made cosmetics will be awarded the "Grand Prix" according to the Secretary General of the Comite du Grand Prix Americain.

In a recent press release, M. Jules du Bois Lambert, Secretary General, said, "The Comite feels that manufacturers of American cosmetics have incorporated in their products and in their advertising the spirit of 'savoir faire' that we French consider so important in our daily lives. Moreover, the beauty aids developed in America have been a boon to women all over the world."

The Comite du Grand Prix Americain was founded to honor American industry for its contributions to better living and to world-wide industry. The Comite will meet quarterly in its headquarters in the Ritz Hotel. At these meetings the products nominated will be evaluated by the Comite with the help of a staff of technical advisers. Actual presentation of the awards will be made at special receptions in the United States attended by dignitaries of Franco-American social, civic, and business life.

Paper clothing is here with a line including shirts, pants, laboratory or shop coats, aprons, hats, overshoes, and medical examination gowns.

A new corporation in New York has just been formed to manufacture disposable paper clothing. The name of the company is Disposables, Inc., and the product will be called Abanda.

Undoubtedly this is progress and will serve a very useful purpose in some factories and laboratories, but our imagination is intrigued at future possibilities.

The longer a customer stays in a store, the more she's exposed to in-store promotions—and the more likely she is to make more and bigger purchases. This is a conclusion from a survey made jointly by the New York University Graduate School of Retailing and the *Variety Store Merchandiser*.

Like a great many things in selling, this seems somewhat obvious, yet, to us this seems to hold all sorts of opportunities for good selling, both to the store and by the store itself.

your product belongs

in glass by Brockway

What makes a product belong? Acceptance by the consumer public . . . acceptance for the product itself . . . and acceptance for the container in which it is presented for sale. • A good product is greatly enhanced at the point of sale when presented in an attractive glass container . . . a glass container by Brockway. • Brockway provides individuality in a glass container . . . the kind of individuality that makes your product stand apart from all the rest, thereby providing a strong advantage at the point of sale. • A product that is worthy of consumer acceptance deserves a quality glass container by Brockway.

SYMBOL OF QUALITY · GLASS CONTAINERS ·

BROCKWAY GLASS
COMPANY, INC., Brockway, Pennsylvania
Sales Offices in Principal Cities

News in Packaging . . .

British Company to Sell Lakso Machines

The Lakso Company, Inc., has completed negotiations with Packaging Machinery (Peters) Limited, Slough-Bucks, England, manufacturers of packaging and special-purpose machinery, for the manufacture and sale of Lakso packaging machines in England and Europe. The agreement involves the rights to build and sell Lakso tablet and capsule counting and filling machines to English and European pharmaceutical manufacturers.

Although Lakso machines are used in a number of foreign countries, this is the first time the equipment has been manufactured elsewhere than in the United States.

August Folding Carton Shipments Down

The upward trend experienced since February in shipments of folding cartons ceased in August. According to the Folding Paper Box Association of America, dollar volume of shipments in that month fell 0.8 per cent below the same month last year, and tonnage was off 3.3 per cent. Even so, cumulative volume through August of this year holds at 3.5 per cent ahead of the first eight months of 1958.

Tube Shipments Up

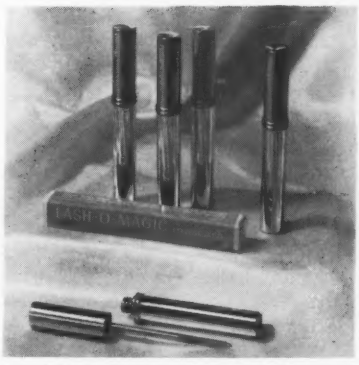
The Collapsible Tube Manufacturers Council has announced that volume of metal tube shipments for the first half of 1959 was nearly 21 per cent above that period in 1958.

Billions of Bottles

The Glass Container Manufacturers Institute has issued a 32-page booklet, Billions of Bottles, which presents the history of the art of making glass from its beginnings, some 25,000 years ago in Egypt, or possibly Mesopotamia, to the present. Well-illustrated with line drawings, the account describes the methods of making glass containers—the sand-core method, the blowpipe, moulding glass, and fully automatic manufacturing—as well as the fundamental developments, for instance, clear glass, transparent colored glass, and glass-of-lead, known as crystal. Famous glass makers are also mentioned, and the glass industry in America receives attention.

The booklet is available from the Institute, 99 Park Avenue, New York 16, N. Y.

Chyman Buccal by Armour Pharmaceutical Company, packaged in short-necked vial glass with molded Polyethylene stopper, both supplied by Demuth Glass Works. Fingers in stopper force tight, positive seal, eliminating any need for the usual cotton filler.



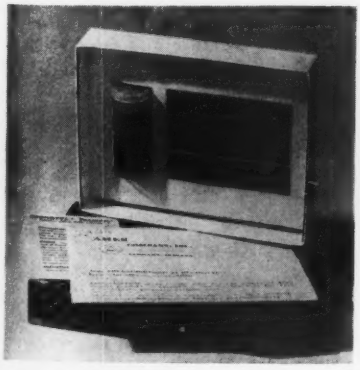
Lash-O-Matic, Barbara Gould's new automatic mascara in sequin shades. Case has brush-gold top, jeweler's gold base with labels duplicating the five shades for identification.

Magi-Care Miniatures by Mytinger & Casselberry, Inc. Sampling device holds mask, lotion, cream in Metalam bags by Dobeckmun Co., division of Dow, with full instructions.

Variety Store Annual Packaging Awards

Among the 1,100 entries in the 23rd Annual Packaging Competition are these cosmetic and toilet goods packages: gold award—Dura-Gloss lipstick, Dura-Gloss Division, Ar. Winarick, Inc.; silver awards—Pic-A-Puff cosmetic cotton, Johnson & Johnson; and Cutex Mira Base, Northam Warren Corporation.

Freescription, mailing to introduce Dechotyl by the Ames Company Inc., and to provide the physician with information and a sample of 14 tablets before they are detailed.



Molded mailer of Pelaspan, a polystyrene foam plastic by Polyfoam Packers Division, Gol-Brite Products, used by Abbott Laboratories. It needs only a label for mailing.

Shelf carton by Irwin, Meisler & Co., for the wholesale trade, with label on both front and 2 side panels, perforated cover and side flaps, and a convenient package divider.

#1

Non-rolling, extra-depth, Bakelite cap; thick-flange rubber bulb; Saftee-ball glass.

#3

Regular plastic cup; thin flange rubber bulb; plastic dropper.

#4

Metal cap; oil - resistant AMEKINE synthetic rubber bulb; blunt glass.

New Modernistic bottle. Designed to lie flat for convenient labeling. Oval front provides ample label space.

New Perfection

DROPPING PARTS

Simplify Your Packaging Problem

The wide variety of sizes, styles and colors in New Perfection's complete line of dropping parts offers the answer to your packaging problem. Each component part is designed to present and administer your product in the most attractive, convenient manner. We supply dropping parts to fit your bottles or furnish the complete unit.

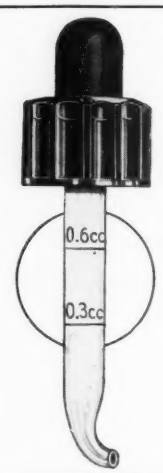
DROPPER GLASSES CAN BE CALIBRATED IN COLOR

An inexpensive extra that adds great convenience to the use of your preparation. The dosage you desire in the color you specify is accurately and permanently printed on the dropper glass. Trade-marks and firm names can also be imprinted.

#2

Non-rolling, extra-depth Bakelite cap; thick-flange rubber bulb; special bent glass, plain or CALIBRATED.

NOTE: Calibration can be applied on plastic dropper.



RUBBER BULBS are supplied in many styles and colors. Oil-resisting AMEKINE synthetic rubber is used for oil preparations; natural rubber is supplied for other products.

CAPS of plastic or metal can be furnished in a complete range of sizes and colors.

DROPPER GLASSES are available in a wide variety of styles and sizes; plain or CALIBRATED in any color to mark specific dosages.

BOTTLES in an attractive modernistic style in Amber, Blue, Green or Clear glass are available in the following sizes: ⅛, ¼, ½, 1 and 2 oz. (Immediate shipment on all sizes and colors.)

We can give prompt service on your special requirements for large or small quantities of droppers made from glass or plastic and in special packaging such as cellophane - wrap.

Write for samples and prices.

PENNSYLVANIA GLASS PRODUCTS CO. INC.

"Glass Goods of the Better Kind"

430 N. CRAIG ST. • PITTSBURGH (13), PA., U.S.A.

NEWS and VIEWS

BY TED KLEIN PUBLIC RELATIONS DIRECTOR*

Media Study

Until recently the main source of information about the composition of a medical journal audience was supplied by publishers' statements of circulation. Occasionally, surveys by individual publications undertook to provide advertisers with additional information on their books.

Last year *Medical Economics* hired Alfred Politz to direct the first major study. It detailed how many physicians read *Medical Economics*, what sort of practices these men have, and how many prescriptions the recipients of the magazine write every day.

Now, another Politz study has been completed—the first well-documented study to compare physician readership of four of the major medical journals: *Medical Economics*, *Modern Medicine*, *MD Medical Newsmagazine*, and *The Journal of The American Medical Association*. The circulation of the above four medical publications reaches an almost identical audience consisting of 137,000 practicing physicians under 65 years of age.

One phase of the study showed that, of the 137,000 physicians who receive the four publications, 71.5 per cent read ME, 62.7 per cent read MM, 56.3 per cent read MD and 54.2 per cent read JAMA regularly. Or, in numbers of readers: ME, 98,100; MM, 86,000; MD, 77,200; JAMA, 74,300. It also shows the readership of various combinations of the four journals.

This study was the result of office interviews with 637 physicians picked by Politz research on a probability sample basis, so that these physicians represent a true sample of American physicians. I estimate that it cost ME about $30,000.

One can draw many conclusions from the Politz study. The most obvious is that the other top publications in the field may be forced to do some serious readership studies. The result will undoubtedly be most helpful to agency people and ad managers, who need this kind of objective analysis in choosing journals.

*Paul Klemtner & Company, Inc.

Squibb's Helping Hand

Kudos of the month are herewith sent to Squibb for their new film "Helping Hands for Julie." In 26 minutes, by means of a 16mm, black-and-white sound movie, Squibb has managed to round up a dozen or so members of the health team who come into contact with Julie, a very sick little girl at the time she is hospitalized.

During the film, shot at Booth Memorial Hospital in Flushing, N. Y., members of the health team are brought into the story as they help Julie recover from her bout with meningitis. Everyone, from admitting resident to the hospital dietitian and the lab technician, is shown as he anxiously plays his part in this typical hospital story.

The atypical part of the story is that the film contains no commercial of any kind from the organization that paid the bills for the production. The film credits show it was produced by the American Medical Association and the American Hospital Association as a public service of E. R. Squibb & Sons. That is the only mention of Squibb.

The main reason for the project, according to Squibb's public relations department, is to encourage young people to seek careers in the health field. Guidance counselors, after they see the film, may be able to see new directions in which to point young people looking for advice in career selection.

This is an excellent example of "pure" public relations—which is invaluable in building and strengthening a corporate image. In paying for this film, Squibb has made, I think, a significant contribution to the health field.

Released in May of last year, "Helping Hands for Julie" has passed the 6,500 mark in bookings and has been seen by 3,362,607 individuals, according to Frank Rollins of Squibb.

In these days of diatribe and invective against the pharmaceutical business, this sort of corporate service must be considered even by its most violent critics as something worthwhile and important.

Lasting Ideas

Friends of the *Reader's Digest* may like to know that the Pleasantville publisher has a beautiful little book called "Lasting Ideas . . . Some Expressions on the Art of Persuasion Wise and Witty Enough to Endure."

We are grateful to Fred Thompson, advertising director of the Digest, who sent us a copy after we had unsuccessfully tried to purloin one.

Typical of some of the comments in the 44 pages is this gem attributed to P. T. Barnum: "Advertise, or the chances are that the sheriff will do it for you."

10,000 Visitors

As soon as Miles Chemical Company of Elkhart, Indiana, was formed, as a subsidiary of Miles Laboratories, H. F. Roderick, president of the company, decided to start his PR efforts with an important event.

The result was an open house during which 10,000 employees, their families, and the towns-people of Elkhart visited the plant. Displays showed the products, plant locations, and personnel policies of the company. The open house was tied in with the 75th anniversary of Miles Laboratories, as well as the formation of Miles Chemical from Sumner Chemical and Takamine Laboratories.

Open house celebrations are always excellent door openers to a community. As Roderick put it, "We feel that our first publics—our employees and the community—now know what we are and how we plan to proceed. The next step is to widen that circle of understanding until it encompasses all our publics."

Ring 4 Times

This reporter has visited his share of office buildings, but not until recently was I in the Broad and Wallace plant of Merck Sharp & Dohme in downtown Philadelphia.

As I was waiting for the elevator, I noticed a little polished bronze plaque placed at the elevator call button stating: "In case of medical emergency, ring 4 times. Repeat if necessary."

I have never seen this before and I congratulate the far-sighted individual in the old Sharp & Dohme plant who made the decision.

Patent thoughts and trends

BY THOMAS CIFELLI, JR., PATENT ATTORNEY*

British Patent Law and Practice

The "One World" of the late Wendell Willkie is certainly not here, a fact which the daily headlines bring home repeatedly. This doctrine is founded on the brotherhood of man and proclaims that the best way to lasting peace is for all peoples to subordinate national jealousies for the greater good of humanity. Efforts in the One World direction are of course always going on; and the United Nations is doubtless the outstanding instrument in this connection.

It may come as a surprise to many that even in such a relatively small field as patents we are still a long way from the One World idea. Indeed, it would seem at times that there are many more patent barriers separating nations than there are barriers in the fields of economics and politics. As a result, if an invention which is truly world-wide in its application is made in any country, it is necessary to file scores of patent applications in as many different countries in order to protect the invention. This is so because, generally speaking, a patent issued by any country affords protection only within the geographical confines of that country.

This situation poses a very difficult practical problem every time an invention is made the subject of a patent application. The question is simply whether any foreign patent applications should be filed and, if so, in what countries. There will be no attempt here to consider the various factors involved in answering that question. However, experience has shown that some countries are selected quite often. These countries include Great Britain, Germany, Canada, and Switzerland. It is therefore felt that a rather cursory look at the patent law and practice in these countries might be of interest and help to the readers of this journal.

Perhaps Great Britain is a good place to begin with. Britain not only has a highly developed chemical industry and represents a large market in itself, but the patent laws of many countries are patterned on the British patent law. What follows represents a very liberal use of the information contained in a paper presented by W. Victor Higgs before the ACS Division of Chemical Literature in 1958 in Chicago, Illinois.

Stages of a British patent application. Just as in the case of a U. S. patent application, the first stage of a British patent application involves examination by the Patent Office, in this case the British Patent Office.

When a British patent application is allowed, it is printed and given a number, but this does not mean that the patent is granted. It is merely opened to the public, and anyone may oppose the grant of a British patent within a specified period. The final stage, the actual grant of a British patent, occurs after the opposition period expires. As in the case of U. S. patents, one cannot sue infringers in Britain until the patent has been granted, but the patentee can recover for infringements which go back to the date of publication.

U. S. concepts vs. British concepts. In the U. S. an inventor is rewarded for 17 years for disclosing his invention in a patent. In Britain the patent right is limited and, if the patent owner does not work the invention, he is liable to lose his rights. Further, the British patent owner must pay taxes each year in order to keep it in force, and these taxes rise throughout the life of the patent from the fifth till the sixteenth and final year. Some other differences between the British and American patents may be of interest. For one thing, in Britain the filing date is the important date, unlike the U. S. situation where the date the invention is made is more important. Also, Britain is not primarily interested in rewarding the *inventor*, as is the case of the U. S. The British system is interested in bringing information into the realm and it matters not who brings the information into the realm. This is shown by the fact that the following persons may be applicants for British patents: (1) the inventor; (2) an assignee of the inventor; (3) the inventor or his assignee in conjunction with others; (4) a convention applicant (which means in effect someone who within the preceding 12 months has applied for a patent in another country belonging to the International Convention, and who will be entitled for priority to his filing date in that other country); or (5) an assignee of a convention applicant.

To the foregoing should also be added anyone who imports the invention into Britain. For this latter reason the names of British patent agents often appear on patents as if they were inventors, although the foreign communicator's name does appear in the published patent specification.

Examination of British patent applications. The examination procedure in Britain is rather similar to that in the U. S. However, British examiners are more restricted as regards the grounds upon which they can reject applications than is the case in the U. S. A. Thus, for example, while a British examiner can reject an application which is completely anticipated, that is, disclosed completely in a publication or patent, the British examiner cannot reject an application for what is called "lack of invention." This latter ground of rejection is perhaps the most often used in the U. S. A., insofar as rejections based on the state of the art are concerned.

Decisions of the Patent Office may be appealed to a Patents Appeal Tribunal who is an especially appointed judge of the High Court.

No interferences in Great Britain. Any inevntors who have had to put up with the involved, time-consuming, and expensive interference proceedings in the U. S. A. will be happy to learn that there is no such aspect to British practice.

*Richards and Cifelli, Newark 2, New Jersey.

Foods and medicines. A special ground of rejection in Britain, which is not employed in the U. S. A., and which is believed to be of interest to the reader, is that patent foods or medicines are not patentable in Britain, if they constitute mere mixtures of known ingredients possessing only the aggregate of the known properties of the ingredients, or a process for producing such substances by mere admixture.

Compulsory licenses. This is another area where U. S. and British practices differ. There is no such thing as a compulsory license in the U. S. However, in Britain, if the invention is not worked or if it is worked substantially entirely by importation from abroad, anyone may apply to the British Patent Office for a compulsory license after three years from the date of sealing of the British patent. It is of interest to note that there are very few reported cases concerning applications for compulsory licenses in Britain.

With respect to the food and medical fields, anyone may apply for a compulsory license at any time after the patent is sealed. There are apparently only two grounds upon which to oppose the grant of compulsory licenses under such patents: (1) that the applicant does not have the manufacturing facilities or know-how to carry out the patented invention; or (2) that the applicant intends to work the invention by importation.

The British Patent Office has the power to set the terms in compulsory licenses. With respect to foods and medicines the terms are to be such that the food or medicament is available to the public at the lowest price consistent with the patentee deriving a reasonable advantage from his patent rights. Higgs believes that it is doubtful whether in the case of drugs the Patent Office would ever agree to a royalty rate sufficiently high to enable the patentee to recoup his cost of research and development.

Extension of British patents. Here too, British patent law is different from U. S. patent law, which does not permit an extension of a patent except by special act of Congress. In Britain it is possible to obtain an extension of the term of a patent after the 16-year period, either on the ground of war loss or on the ground of inadequate remuneration for the invention.

Infringement actions. Just as there are infringements in the U. S. A. there are such things in Britain. However, although infringement suits are expensive in Britain, they are said to involve neither the degree of expense nor the dislocation of business which is true of U. S. actions. A reason suggested by Higgs for this difference is that British infringement actions are heard by a specially appointed judge and one does not have to begin by instructing the judge in patent law or fundamental scientific principles. Also, according to Higgs, British courts restrict themselves closely to the issues of infringement and validity. Other considerations, such as what are often termed the equities and the patent owner's business history in relation to the patent are not considered. Infringement actions are heard by a judge of the High Court. The judge is in practice the same person who is Patents Appeal Tribunal which hears appeals from the decisions of the Patent Office.

The Role of Patents and The Growth of New Companies

Dr. Edwin H. Land is widely known as that rare combination of person: one who has the creative mind of an inventor and the business mind of a successful corporate manager. As such the views of the President of Polaroid Corporation seem to be entitled to much weight and respect. His views as recently presented and reported are summarized in what follows.

It is not surprising that one who created not only a new company but a new industry, as did Dr. Land, feels something less than affection for large and fundamentally uncreative companies. Dr. Land feels that to such companies a patent system poses a threat and is a nuisance.

In contrast to large and uncreative companies, there are large and very creative companies, which in Dr. Land's view are entitled to be called "great." These companies are the big companies whose whole concept of a good future involves feeding into their manufacturing departments and into their distribution channels products so new and deriving so directly from the latest ventures in pure science that the management of these companies will not be sure today what the products of tomorrow are going to be. These companies are basing their choice of products from year to year on what *new* discoveries fit best into the satisfaction of *newly* sensed needs of the American market.

To such "great" companies Dr. Land feels that patents are a vital protection for their continued right to manufacture. Dr. Land feels that no one today can run the risk of creating a new section of industry without absolute conviction that the substance of contributions he has made to a field justified the patents he received and without full knowledge that the form of the disclosure, the adequacy of the disclosure, and the thoroughness of examination were such that, if the patent on which the company based its new industry were ever brought into contest, the company could go into a court with sureness, with a kind of confidence that can be transmitted in the atmosphere of a court room only when it is apparent that the inventors know their field, know its history, know the great fundamental problem and know, most of all, that to this field they have brought genuine creativity. The drive on the part of a large creative corporation is, therefore, to disclose early, to disclose fully, to disclose confidently; and Dr. Land feels that without the patent system this drive would be removed and this information would be concealed.

One often overlooked advantage of large creative corporations is that they enable the young men who staff their laboratories to satisfy their urge to explore the scientific frontiers. This is because scientists are permitted to participate in advancing scientific knowledge while at the same time the corporation supporting them is protected by patents obtained on their inventions. The scientific world is continuously being repaid by the prompt publication, both in patents and in scientific journals of the new findings. The alternative to all of this is what Dr. Land refers to as the "cesspool of secrecy, an industrial environ-

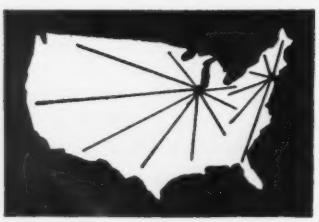
(*Continued on page 506*)

GET THE FACTS ABOUT THE MANY ADVANTAGES OF G. BARR & COMPANY TWO-PLANT AEROSOL PACKAGING SERVICE

In New York—as in Chicago—you can enjoy the outstanding research, product development and precision aerosol packaging service of a G. Barr & Company *local* plant and also share in the *many advantages* of G. Barr & Company *two-plant* operation.

Among these advantages are the potential savings in both shipping and production costs. You also enjoy the benefits of our unsurpassed laboratory facilities, of our two-plant buying power, our time-tested quality controls and the important know-how gained over the years in the production of hundreds of millions of aerosol packages.

There are many other important pluses which *only* G. Barr & Company can offer. We would like to tell you about them, at your convenience and without obligation. Just contact our nearest office for facts.



NEW YORK
4747 Bronx Blvd.
FAirbanks 5-7870

CHICAGO
3601 S. Racine
YArds 7-1700

G. BARR & COMPANY
PRIVATE LABEL AEROSOLS

OPAL . . . the aristocrat of glass

Here indeed is the glass container at its finest . . . sparkling, white opal made to Carr-Lowrey's superior standards of excellence.

The bottle #100, and the jar, #447, provide unsurpassed packaging possibilities for an exceptionally wide range of products. Number 100 is presently available in 4, 6 and 8 ounce sizes. Number 447 in 1, 2, 4 and 8 ounces. All can be supplied plain or decorated to your specifications.

Designers and manufacturers of fine glass containers

Factory and Main Office: BALTIMORE 3, MD. • New York Office: 415 MADISON AVE. • Chicago Office: 1572 MERCHANDISE MART

Richard Groben, Regional Sales Manager (left) and Edwin Pomerantz, Pharmaceutical Section, Technical Service Department, discuss a customer's Vitamin C formulation problem.

Question:

WHAT'S BEHIND PFIZER C?

Answer:

PFIZER TECHNICAL SERVICE.

How a Customer Was Able to Lick a Tough Production Problem Without Buying Special Equipment.

● A potential customer recently called Pfizer with a problem. He was trying to make a small, high potency vitamin C tablet by the wet granulation technique. However, he ran into severe discoloration using his standard forced-air dryer.

When he tried to solve this problem using double compression, he got a tablet that was too large. He could buy vacuum drying equipment. But that would be expensive.

At this point he called Pfizer for help.

He was advised to use Pfizer ethylcellulose-coated ascorbic and to granulate with starch paste. The potential customer was then able to produce the tablet he wanted with his own conventional drying equipment (also at this point, he stopped being a potential customer and became a regular Pfizer customer for Vitamin C). The ethylcellulose coating prevented the ascorbic acid from reacting with moisture to the extent that discoloration was avoided.

Data from subsequent accelerated stability tests run by Pfizer enabled the customer to proceed with production and sales.

Here again is a case history of a satisfied Pfizer bulk medicinal customer. One of the many who has taken profitable advantage of Pfizer's 22 years experience with vitamins. You, too, will be satisfied if you come to Pfizer with your Vitamin C needs.

Pfizer offers six U.S.P. forms of ascorbic acid plus a special grade for use in parenterals, ascorbic acid U.S.P. AA grade. Also in the Pfizer Vitamin C line are: ascorbic acid, coated—sodium ascorbate—calcium ascorbate—ascorbyl palmitate.

Pfizer offers the following technical assistance on vitamin C:

1. Formulation information on new products
2. Cooperative stability studies on your product during developmental stages
3. Check-assays during product development
4. Technical literature
5. Trouble shooting on existing products

The Chemical Sales Division's bulk medicinal line includes vitamins (A, B-complex, C), antibiotics, hydrocortisone, caffeine, L-Lysine, etc. Behind all of these stands Pfizer's Technical Service.

CHAS. PFIZER & CO., INC.
Chemical Sales Division
630 Flushing Ave., Brooklyn 6, N.Y.

Branch Offices: Chicago, Ill.; San Francisco, Calif.; Vernon, Calif.; Atlanta, Ga.; Dallas, Tex.

Pioneer in the Manufacture of Vitamins

Pfizer

Left to right: Harold F. Cummings, vice-president, Pitman-Moore Company; Benjamin F. DeHays, Jr., manager, product addition studies department, Eli Lilly and Company; G. Sterling Brady, director of market research, Bristol-Myers Products Division; and Carl Goldschrafe, mid-western sales representative, Fleuroma, Inc., with sales offices in The Pittsfield Building, 55 East Washington, Chicago 2, Illinois.

NEWS...

Appointments and Promotions

Harold F. Cummings has been appointed vice-president by the **Pitman-Moore Company.** Mr. Cummings had been with the Vitamerican Corporation since 1948, as vice-president in charge of sales.

Eli Lilly and Company has appointed Harold M. Wisely, Ph.D., director of its new export affiliate, **Eli Lilly International Corporation.** Within the division, a personnel planning department with Russel C. Hagerman as manager has been established. Dr. Wisely has served as assistant director of personnel planning and coordination for Lilly; Mr. Hagerman has been in the field of industrial relations for the parent company for ten years, since 1957 as chief of the personnel department at the Kentucky Avenue plant. Oscar W. Funk, vice-president and general manager of **Eli Lilly and Company (Canada) Limited** since 1955, has been elected president, by its board of directors. He has been with the company for 32 years. New manager of Eli Lilly and Company's product addition studies department is Benjamin F. DeHays, Jr., who succeeds William D. Cairns, recently named manager of the Boston district. Mr. DeHays has been medical projects co-ordinator, medical administrative division.

G. Sterling Brady has been appointed director, market research, by **Bristol-Myers Products Division.** He succeeds Alfred A. Whittaker, who is now vice-president in charge of advertising. Mr. Brady had been director of market research with General Foods.

Fleuroma, Inc. has appointed Carl Goldschrafe as mid-western sales representative, with offices in Chicago. He was formerly with Helene Curtis Industries, Inc.

Charles H. Pressel, vice-president in charge of production, **Burroughs Wellcome & Company (U.S.A.), Inc.,** has been elected a director. Mr. Pressel has been with the firm since 1939.

Dr. Harold E. Zaugg has been named research fellow, and Dr. Frederick N. Minard, research associate, two newly created positions at **Abbott Laboratories.** Dr. Zaugg has been with Abbott since 1941, and Dr. Minard since 1944. Manager of three buying divisions in the purchasing department have also been appointed: Jack C. Bell, in the department since 1950, now manager, equipment and supplies purchases; Eugene F. Swanson, with purchasing since 1950, is manager, chemical purchases; and Daniel L. Yocum, Jr., is manager, packaging materials purchases. Mr. Yocum, with Abbott since 1939, has served most recently as senior buyer, packaging materials.

George B. Christian, Jr., has been named government representative of the **Tailby-Nason Company,** a newly created position. Mr. Christian has represented a number of pharmaceutical companies in Washington in the past ten years

Donald A. Bandman has been named assistant brand manager in the **Lehn and Fink Division, Lehn and Fink Products Corporation.** He was formerly an assistant brand manager for Procter and Gamble. In the **Tussy Division,** Robert Muecke has been named advertising manager. Mr. Muecke had been sales promotion manager for the division.

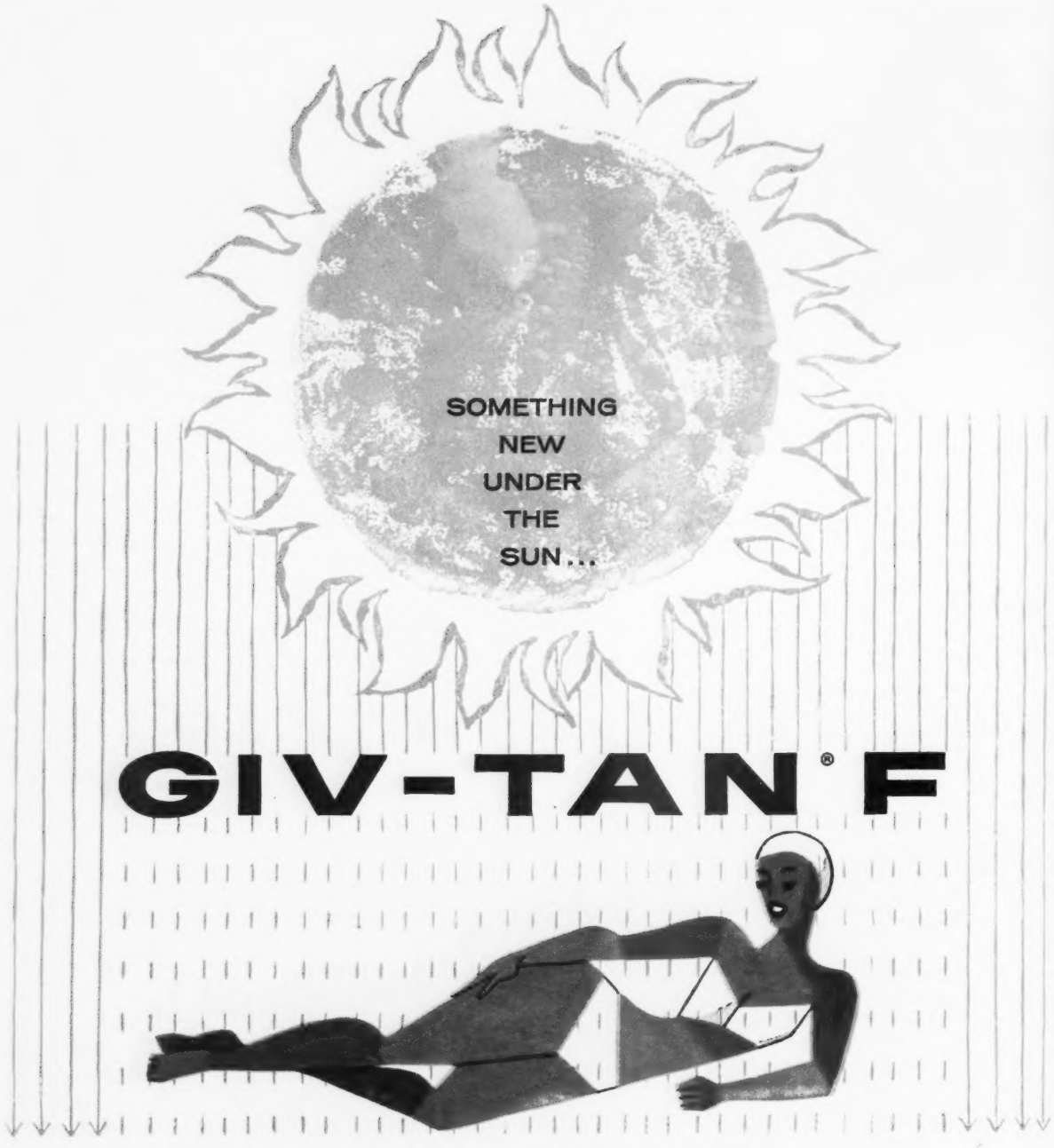
Kenneth W. Keller, formerly director of retail marketing for the LePage Division, Johnson & Johnson, has been named director of merchandising and promotion, **Warner-Lambert Products Division of Warner-Lambert Pharmaceutical Company.** Gerard S. Fowler has been appointed general manager of Hawaiian operations for the pharmaceutical company. He was formerly executive vice-president, Family Products Division.

Ungerer & Company, Inc., has appointed F. J. Hailer, Jr., to represent the firm in New England. Mr. Hailer succeeds the late Warren G. Kell.

Fred Lean has been named vice-president and general manager of **Miles California Company,** succeeding Frank G. Clancy, who has retired. Mr. Lean joined Miles 19 years ago as office boy under Mr. Clancy.

John A. Cawley has been appointed president, and Edwin F. Roberts vice-president, of **Ives - Cameron Company, Division of American Home Products Corporation.**

Dr. Joseph G. Greslin has become research and technical director at **Lloyd, Dabney & Westerfield, Inc.** Dr. Greslin was formerly associated with the scientific division, Wm. S. Merrell Company, and had done research at Merck Institute for Therapeutic Research.



GIV-TAN F is a new sunscreening agent developed by Sindar's research laboratories to increase the efficiency and sales appeal of your suntan product. It enables you to provide maximum sunburn protection—and the deep, lasting, bronze-like tan your customers want—at savings up to 50%!

GIV-TAN F is easy to use. Being a miscible oil, it dissolves and mixes readily in all media normally employed for sunscreen preparations. As an oil it offers special qualities that enhance the cosmetic elegance of your product.

GIV-TAN F is stable in solution and under exposure to sunlight...proved in field and laboratory tests...harmless to fabrics...non-irritating to the skin. It is extremely economical in any type of suntan preparation or sunburn preventive—in hydro-alcoholic solutions, oils, lotions, creams and other products.

We are ready to give you complete information on GIV-TAN F and full cooperation in using it to the best advantage in your preparations.

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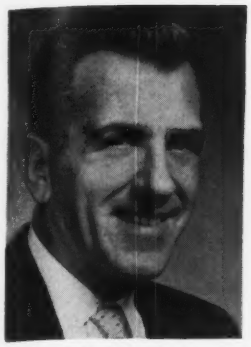


Left to right: John F. Barry sales engineer, Arthur Colton Company; R. W. Betzing, assistant merchandising manager, E. R. Squibb & Sons;

Norman H. Blumberg, manager, organization and development, Merck & Co., Inc.; Edward Onyskow, sales representative, Dodge & Olcott, Inc.

John F. Barry, a sales and service engineer for the Hope Machine Company for more than 13 years, has been appointed sales engineer in the New York district office of the **Arthur Colton Company.**

E. R. Squibb & Sons has appointed R. W. Betzing assistant merchandizing manager. Mr. Betzing joined Squibb in 1951 as a sales representative in the Detroit area. Arthur W. Willis, plant manager for the New Brunswick manufacturing laboratories, has taken on additional responsibility as assistant director of manufacturing operations, a newly created position. Dr. L. Ravaris has become an assistant medical director of the company. During the past year he has served as a rotating intern at Henry Ford Hospital in Detroit, Mich.

Merck & Company, Inc., has created a new position, manager of organization and development, to which Norman H. Blumberg has been appointed. With Merck since 1939, he has been a director of systems and data processing since 1957, when he also served as acting treasurer of the firm's Canadian subsidiary.

Edward Onyskow, who has joined the ranks of **Dodge & Olcott, Inc.,** as sales representative in the New York area, began with D&O in 1953 as an analytical chemist, then served as research chemist.

Vernon L. Luttrell has been appointed national wholesaler sales manager of **Park & Tilford, Toiletries Division.** Mr. Luttrell previously was general sales manager at Pure Pac Corporation, and has been national wholesaler sales manager for several years at Lentheric.

The new head of the foreign law section in the legal department of **Sterling Drug, Inc.,** is Andrew P. Power, succeeding Victor C. Folsom, who has been named assistant general counsel of the **United Fruit** Company. Mr. Power has served in the foreign law section since joining Sterling in 1952.

The Dow Chemical Company has formed a new Allied Industries group to administer its activities in coating materials. L. H. Silvernail has been advanced to the position of manager of the group, which will be responsible for the company's Coatings Technical Service work. J. P. Strasser, former custom service chemist, is in charge of the new textile section; E. J. Heiser has been promoted from customer service chemist to head the paper section; Ralph C. Hand, formerly head of the textile section, is now head of the building products section; and F. R. Lehman heads the packaging section, which is to implement the flexible packaging work of the firm.

The Robinson-Wagner Company, Inc., has appointed Thomas O. McNearney, Jr., as sales representative for the St. Louis-Memphis area.

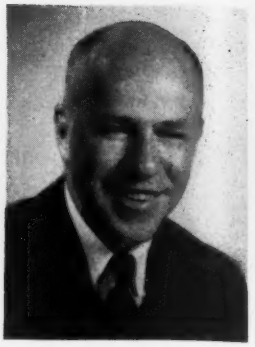
Adele Berger has been appointed product manager by **Max Factor & Company.** She will be in charge of the firm's treatment line. Prior to her new position, Miss Berger was associated with a New York cosmetic company.

Robert D. Stewart, a technical representative in the New Chemicals Division, has been appointed market analyst in the market research department of **Union Carbide Chemicals Company, Division of Union Carbide Corporation.** New assignments for five men in the sales department have also been announced: technical representative Arthur A. Boucher, transferred to the New York district from Buffalo; Malcolm H. Mackay, technical representative, transferred from Newark to the Buffalo district; and, assigned as technical representatives after completion of the sales training program are William R. Britton, to the Moorestown, N. J. district; Donald M. Sullivan to the Cleveland district; and Frank S. Wimer to the Newark District.

Three scientists have joined the research staff of **Chas. Pfizer & Company, Inc.** at the Maywood, N. J., laboratories. Dr. William H. Funderburk, senior neuropharmacologist, and Josep Garcia Llaurado, M.D., endocrinologist, are now associated with the macrobiological laboratories, which are soon to be moved to the research center being completed in Groton, Conn. Dr. Funderburk had been a pharmacologist with Miles Research Laboratories. Dr. Llaurado formerly had a U. S. Public Health Post Doctorate fellowship in the Biochemistry Department of the University of Utah College of Medicine. He received his M.D. degree from the Medical School of the University of Barcelona, Spain. Mr. Carleton has been group leader in radiochemistry with the National Dairy Products Corporation for the past nine years.

Revlon, Inc., has appointed Lester Herzog general manager of the Bressard Tiara hair color products division. He has been with Revlon for 20 years.

Left to right: L. G. Cannella, product sales manager, non-food cans, and C. L. Elliott, acting manager, Passaic plant, Continental Can Company; Frank H. Pratt, director, sales, and Douglas E. Ward, director, marketing research and development, Ciba Pharmaceutical Products, Inc.



L. G. Cannella has been appointed products sales manager of non-foods for the Metal Division of the **Continental Can Company.** He is succeeded in his former position as district sales manager for metal containers in New York City by T. V. Carley, previously in a comparable position in Boston. C. L. Elliott, assistant manager of the firm's Houston, Texas, can plant, has become acting manager of the Passaic, N. J., can plant.

Ciba Pharmaceutical Products, Inc. has appointed Frank H. Pratt to the newly created position of director of sales, and Douglas E. Ward to the newly created position of director of marketing research and development. Mr. Pratt has been with the firm since 1940, as sales manager since 1946, and Mr. Ward, director of marketing research since 1950, has been with Ciba since 1945. Other changes include Sidney J. Jackson, formerly assistant sales promotion manager, to sales promotion manager; Lawrence H. Zahn, manager of methods and package development division, to director of a newly created purchasing and package development division; Dr. Roy Kuramoto, manufacturing pharmacist in charge of special projects, to director of the pharmaceutical manufacturing division, which has been reorganized; Paul H. Schulz, assistant manager for pharmaceutical operations, to manager of the package development and procurement section; Howard M. Bilden, sales promotion manager, to the newly created position of assistant director of sales; Ben A. Bentley, eastern division manager, to the newly created position of field sales manager; George Brenneman, district manager, to eastern regional manager; and Herbert Erger, sales training associate, to manager of the Rochester district.

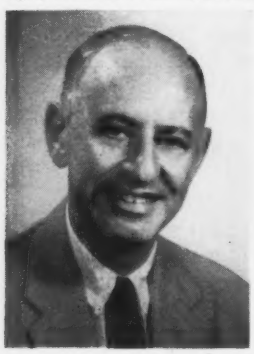
Syntex has appointed a physician, Dr. Jose Steinhardt, as manager of their new Division Pharmaceutica, which is to operate initially in Mexico only. Dr. Steinhardt, before joining Syntex a short time ago, was with Laboratories Hormona, in Mexico City.

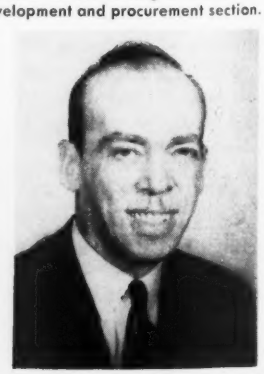
Walter J. Kilmer has been made manager of the Detroit sales division for **U. S. Industrial Chemicals Company, Division of National Distillers and Chemical Corporation.** He succeeds Fred M. Henley, who is retiring after more than 35 years with U.S.I., serving since 1936 as division sales manager. Mr. Kilmer has been with the firm for about 25 years.

Philip Lisbon has been named merchandising manager, cosmetics and toiletries, for the **Rexall Drug Company.** He was formerly director of package development for Max Factor & Company.

Dr. Robert T. Stormont, former director of the department of therapy and research of the American Medical Association, has become vice-president of the **Vick Chemical Company.** Vick's new research director is Dr. Chester E. Poetsch, formerly head of the pharmaceutical chemistry section of Smith, Kline & French. He is vice-president-research for both Vick Products Division and Vick International Division, with headquarters in the new laboratory in Mt. Vernon, N. Y. Dr. Michael Hawksley has been appointed director of biological production for **Jensen-Salsbery Laboratories, Inc.,** a subsidiary, in Kansas City. Dr. Hawksley had been head of production at Bayer Biological Institute in London, England.

Left to right: all of Ciba, Sidney J. Jackson, sales promotion manager; Lawrence H. Zahn, director, purchasing and package development; Dr. Roy Kuramoto, director, pharmaceutical manufacturing division; and Paul H. Schulz, manager, package development and procurement section.





From left to right: Davis Philipson, now director of purchasing, Aerosol Techniques, Inc.; Robert W. Coughlin, assistant sales manager, Pneumatic Scale Corporation, Ltd., with offices in Quincy, Mass.; Dr. Souren

Avakian, director of research, Denver Chemical Manufacturing Company; and W. B. Van Alstyne, Jr., administrative vice-president in charge of coordination of operations, Bard Pharmceuticals, Inc.

Davis Philipson has been promoted from the position of assistant director of purchasing to that of director of purchasing at **Aerosol Techniques, Inc.** The company has also announced that Fay Mowery Moore, has become design consultant. Miss Moore has been associated formerly with Bonwit Teller, B. H. Wragge, and the Carnegie Institute of Technology and Yale University.

Robert W. Coughlin has become assistant sales manager for **Pneumatic Scale Corporation, Ltd.** He joined the firm in 1949 and since 1951 has represented the company in the midwest.

The Denver Chemical Manufacturing Company Has appointed Dr. Souren Avakian director of research. He will direct the company's expanding research and development program in the ethical and proprietary drug field. Most recently assistant research director in charge of organic research for National Drug Company, Dr. Avakian has published extensively and holds numerous patents in organic chemistry.

W. B. Van Alstyne, Jr., has joined **Bard Pharmaceuticals, Inc.,** as administrative vice-president in charge of coordination of operations. Dr. Van Alstyne has spent 25 years with Merck and Company, Inc., most recently as assistant to the corporate executive vice-president at New Jersey headquarters.

Ungerer's Vice-President Returns

William H. Dunney, Jr., vice-president and director of the fragrance laboratories for Ungerer & Company, Inc., has just returned from a business trip to the Northwest and Canada.

Steinhardt Heads New Syntex Division

Syntex has appointed Dr. Jose Steinhardt, a physician well-known in Latin America for his work in steroids, as manager of their new pharmaceutical division, which will initially operate exclusively in Mexico.

Dr. Steinhardt left Vienna in 1938 to enter the drug field with Laboratories Hormona, whose headquarters are in Mexico City. He recently joined Syntex.

The new organization, Division Pharmaceutica, has already trained 40 salesmen, and is clearing ground for a new plant. A pilot laboratory is now operating, and a temporary program handles ethical sales.

Stanley Clark Elected

Stanley I. Clark, vice-president of Sterling Drug, Inc., and executive vice-president of its Glenbrook Laboratories Division, has been elected vice-president of the New York Board of Trade.

Mr. Clark has served on the organization's board of directors since 1948, and was president of the Drug, Chemical and Allied Trades Section from 1953 to 1954. He has been with Sterling Drug since 1943.

Canadian I.F. & F. Consolidated in Toronto

The flavor and fragrance operations of International Flavors & Fragrances (Canada) Ltd. are now consolidated at one location in Toronto, under the direction of Fred Crowhurst, vice-president. This move, according to Charles P. Walker, president of International Flavors & Fragrances, Inc., will facilitate serving the Canadian market.

Veterinary Association Installs Scheidy of SKF

Dr. Samuel Scheidy, veterinary medical director of Smith Kline & French, has been installed as president of the American Veterinary Medical Association, during its 96th annual meeting in Kansas City, Mo., which was held in conjunction with the third Pan American Veterinary Congress.

A member of the AVMA executive board for 16 years, Dr. Scheidy has been associated with SKF's Animal Health Products Department since 1957. He is currently assistant professor in clinical veterinary medicine at the University of Pennsylvania.

Lilly's New Division

A new division, International Personnel and Public Relations, has been created by Eli Lilly and Company's export affiliate, Eli Lilly International Corporation. Harold M. Wisely, Ph.D., is the director.

The new division will establish and maintain personnel and public relations functions at the export subsidiaries in England, Canada, Mexico, Argentina, Brazil, India, Colombia, Australia, and Italy.

Within the division, a personnel planning department has been established, with Russell C. Hagerman as manager.

Since 1957 Dr. Wisely has been assistant director of personnel planning and coordination for Lilly. He joined the firm in 1947 as chief of personnel testing.

Mr. Hagerman has been working in industrial relations for the parent company for ten years, since 1957 as chief of the personnel department at the Kentucky Ave. plant.

SILICONE NEWS from Dow Corning

Wrap Her Up With Silicones

Result: when a cosmetic contains Dow Corning Silicones, it has a more pleasing effect, protects and lasts better in use. When you sell pleasing softness and lasting protection, the sale's pretty well wrapped up. And when you wrap your customers in this lasting protection, you've made lasting friends . . . repeat sales are a cinch.

Why not investigate these unusually effective ingredients? Dow Corning cosmetic chemists have developed silicones specifically for the cosmetics industry, and have amassed a tremendous amount of information on the behavior of silicones in various formulations. Technical assistance is yours for the asking. Dept. 1122.

For Surer Cosmetic Sales, Add Dow Corning Silicones

Whether your product is a hand cream, hair spray, sun-tan oil, baby lotion or other preparation, you and your customers stand to profit if you include Dow Corning Silicones in your formula. Every day, at every turn, more and more women are learning that the word "silicones" on a label means better and longer protection, greater softness.

Why so? Because silicones strongly resist being washed away, they overcome the problem common to most cosmetics — lack of wash resistance. Silicones repel water-borne irritants, too, without interfering in the least with the skin's need to "breathe".

Never oily or sticky, Dow Corning silicone fluids, for example, help the spreading characteristics of a lotion . . . enable it to be worked into the skin more easily . . . provide a softer skin and a fresher, smoother feeling.

Your nearest Dow Corning office is the number one source for information and technical service on silicones.

first in silicones

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W. Huisking Elected DCAT President

William W. Huisking, president of Chas. L. Huisking & Company, Inc., was elected president of the Drug, Chemical and Allied Trades Association during the recent annual convention at the Sagamore Hotel, Lake George, New York.

WILLIAM W. HUISKING

Other officers elected are James Day, Dow Chemical Company, vice-president; William J. Schieffelin, III, Schieffelin & Company, treasurer; William J. Quinn, Merck & Company, Inc., counsel; and Helen L. Booth, executive secretary.

Ralph A. Clark, retiring president, announced during the convention that the name of the organization has been changed from Section to Association.

Four hundred and eighty members and their wives heard Stacey H. Widdicombe, program associate of the Ford Foundation, speak on business executive retirement and the old age problem, and Ward Jackson of Commercial Solvents discuss product and liability insurance.

Frank G. Clancy Retires

Frank G. Clancy, vice-president and general manager of Miles California Company for the past 27 years, was honored recently at a retirement party at the Beverly Hills Hotel by officials in California industry and of Miles Laboratories, Inc., Elkhart, Indiana.

Mr. Clancy opened the western states division of Miles in 1932, with a staff of two—himself and a secretary. It now has a staff of 30.

Fred Lean, who joined the division 19 years ago as office boy, has been named to succeed Mr. Clancy as vice-president and general manager.

Dr. Hoejenbos Celebrates 40 Years with Polak's Frutal Works

Dr. Leendert Hoejenbos, managing director of Polak's Frutal Works, N. V., Amersfoort (Holland), associated company of Polak's Frutal Works, Inc., Middletown, N. Y., recently celebrated his fortieth year with the company. His associates honored him with a dinner, and Jacob Polak, chairman of the board and one of the co-founders of the company, presented him with a pair of antique silver chalices. Personal gifts from many friends were also presented, as well as testimonials from J. E. Meihuizen, co-director of the Amersfoort firm and R. de Kat, managing director of Soflor, Ltd., Perivale (England), an associated company. Mr. de Kat himself had celebrated 40 years with the firm two months earlier.

In 1931, at the death of Henry Polak, Dr. Hoejenbos took over the technical management of the firm and, in 1940, when the Polak family moved to the United States, he assumed the over-all management of the company.

Dr. Hoejenbos has published a number of articles on flavoring and aromatic materials, of which the best known is his work with the late Dr. Coppens on the constituents of raspberry and strawberry juice.

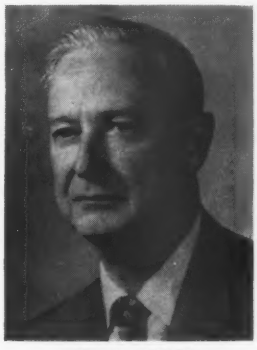
Ives-Cameron Moves to New York City

The administrative offices of the Ives-Cameron Company, a division of American Home Products Corporation, have been moved from Radnor, Penna., to 260 Madison Avenue, New York City.

Fred M. Henley Retires from U. S. Industrial Chemicals

Fred M. Henley has retired from his position as manager of the Detroit Sales Division of U. S. Industrial Chemicals Company, Division of National Distillers and Chemical Corporation.

Mr. Henley joined U.S.I. in 1923



FRED M. HENLEY

at the company's Baltimore Research Laboratory. In the following year, he became a salesman at St. Louis, and then, in 1936, he went to Detroit, where he remained until his recent retirement.

Chesebrough-Pond's Executives Executives Touring Africa

Henry Herbert, vice-president, Chesebrough-Pond's International Division, and Charles Quigley, advertising manager for the division, are touring Africa. They plan to visit Nigeria, Ghana, South Africa, and Salisbury and Bulawayo in the Central African Federation.

Mr. Herbert will then return to the U.S.A., and Mr. Quigley will meet with company executives in England and Switzerland.

Honoring Frank G. Clancy (left) for 27 years as vice-president and general manager, Miles California Company, on his retirement: C. S. Beardsley, chairman of the board, Miles Laboratories; Mrs. Lewis Bonham; Mr. Bonham, president, Miles Products Division; Shirley Mills. Shirley Mills.

VITAMINS by the TONS

Come RIGHT from ROCHE

- **Vitamin A**
  Palmitate and Acetate
  (liquid and dry forms)
- **Beta Carotene**
  (crystals, suspensions & dry beadlets)
- **Vitamin B_1**
  Thiamine Hydrochloride
  (regular and ampul types)
  Thiamine Mononitrate
- **Vitamin B_2**
  Riboflavin
  (regular and solutions types)
- **Riboflavin-5′-Phosphate Sodium**
- ***dl*-Panthenol** ***d*-Panthenol**
  ***d*-Calcium Panthothenate**
- **Vitamin B_6**
  Pyridoxine Hydrochloride
- **Niacin — Niacinamide**
- **Biotin**
- **Vitamin C**
  l-Ascorbic Acid Sodium *l*-Ascorbate
  Coated *l*-Ascorbic Acid
  Sodium Erythorbate Erythorbic Acid
- **Vitamin E**
  dl-alpha-Tocopherol (yl) Acetate
  dl-alpha-Tocopherol unesterified
  Dry Vitamin E Acetate 33⅓% and 25%

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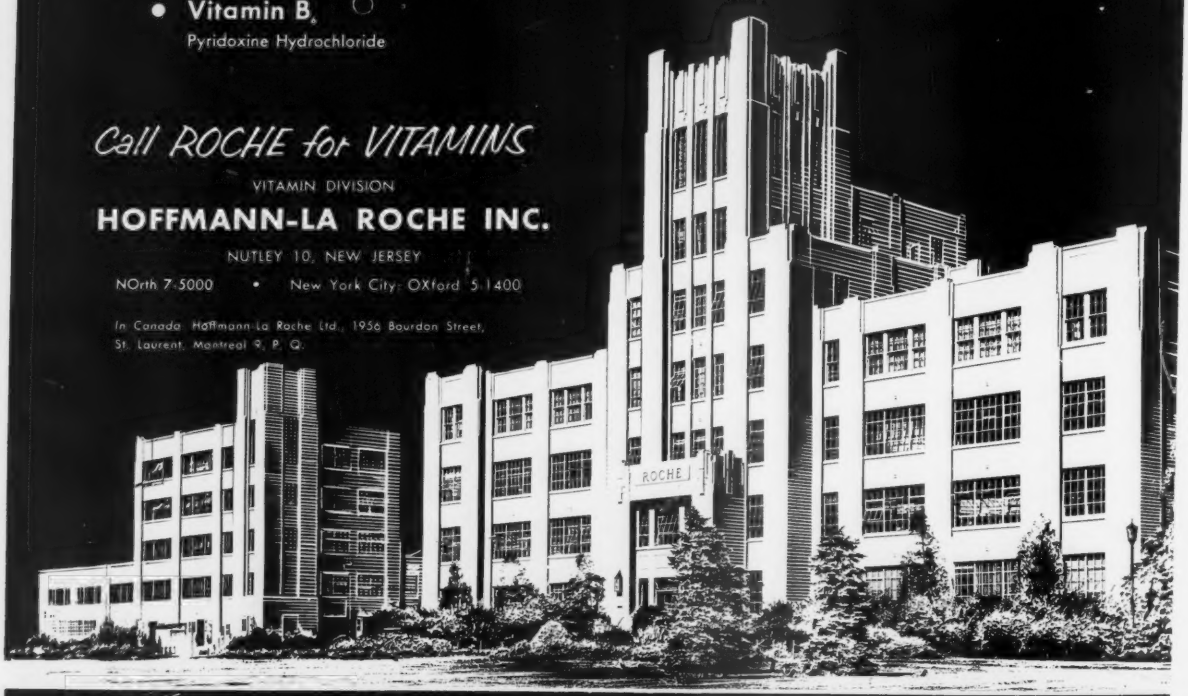


RIGHT FROM ROCHE

Miles California Vice-President Retires

Frank G. Clancy, vice-president and general manager of Miles California Company for the past 27 years, was honored recently at a retirement party at the Beverly Hills Hotel attended by key figures in Southern California media and drug fields, and officials of Miles Laboratories, Inc., Elkhart, Ind.

Mr. Clancy opened the western states division of Miles in 1932, with a staff of one—his secretary. Now, 27 years later, the division has a staff of 30.

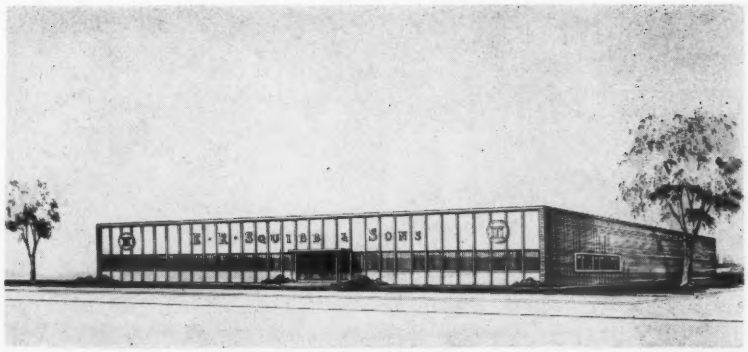
Fred Lean, who joined the Miles California Company 19 years ago as office boy, has been named to succeed Mr. Clancy as vice-president and general manager.

Geiling Joins FDA

D. E. M. K. Geiling, former Frank Hixon Distinguished Service Professor of Pharmacology at the University of Chicago, has been appointed to the staff of the U. S. Food and Drug Administration. He is to serve as Medical Officer and head of the Pharmacodynamics Branch of the FDA's Division of Pharmacology, where his responsibilities will include testing and evaluating safety data for new drugs, pesticide chemicals, food additives, coal tar colors, and cosmetics.

P.M.A. Moves

The Pharmaceutical Manufacturers Association has moved its offices to 1411 K Street, N.W., Washington 5, D. C. The telephone remains the same, NAtional 8-6435. Dr. J. O'Neill Closs, administrative vice-president, is now located at the Washington office, and the New York office has been closed.



Architect's rendering of million-dollar branch facility to be constructed by E. R. Squibb & Sons at junction of Buffalo Speedway and W. Alabama Ave., Houston, Texas, for occupancy early in 1960. It will provide 40,000 square feet for office, warehouse, and shipping services.

A.Ph.A. Elects Loynd

Harry J. Loynd, president of Parke, Davis & Company, was elected honorary president of the American Pharmaceutical Association for 1959-1960, during the association's 106th annual convention.

Mr. Loynd joined Parke, Davis in 1931, and rose rapidly until, in 1945, he was named vice-president in charge of domestic and Canadian sales and promotion. In 1946 he was elected to the board, and five years later became president.

Representative Curtis Addresses Missouri Group

During its monthly luncheon in October, the Associated Drug and Chemical Industries of Missouri heard the Honorable Thomas B. Curtis, Representative from the Second Congressional District of Missouri, speak on the fight against inflation. Mr. Curtis is a member of the House Ways and Means Committee, and a ranking minority member of the Joint Economic Committee, with a major role in legislation dealing with taxation, fiscal policies, and military procurement.

D. W. Cook Retires

D. W. Cook, vice-president and general manager of the New York Division, S. E. Massengill Company, has retired, although he remains with the firm in an advisory capacity. He began with Massengill in 1921.

The retirement was announced at a dinner held during a company marketing and executives' conference held recently in Roanoke, Virginia.

Parke-Davis Is Building

Parke, Davis & Company has purchased a three-acre site in Brook Hollow Industrial Park, Dallas, Texas, for the construction of a new distribution center. Completion is scheduled for mid-1960, when the new building will replace the firm's present facilities at 2820 Taylor Street.

Colgate Establishing New Research Center

The Colgate-Palmolive Company has announced plans to establish a multi-million dollar center for basic and applied research adjacent to the Rutgers University Science campus at New Brunswick, N. J.

The 200,000 square-foot area will be constructed on a 75-acre tract bordering the University's science center, which will further the already existing close relationship between Colgate and the University in several fundamental research programs.

The center is expected to be ready for use in late 1961, when it will house the biological and dental research groups, as well as other research sections of the firm.

Colgate-Palmolive Company's projected center: two main laboratory wings 250 feet long at the rear, three smaller wings in front for administration, library, seminar room, cafeteria.

SCENTS
OLAK'S RUTAL ORKS INC., MIDDLETOWN, N.Y.
AMERSFOORT, HOLLAND · PARIS, FRANCE · BREMEN, GERMANY · BRUSSELS, BELGIUM · SOFLOR LTD. - PERIVALE, ENGLAND

New Quarters for Anchor Hocking Division

The Anchor Hocking Glass Corporation has moved its Detroit Package Division to larger quarters at 17500 W. Eight Mile Road, Detroit 35, Mich.; telephones, KEnwood 7-7730 and ELgin 6-8500.

For the convenience of customers calling at the new office, a display of Anchorglass containers and the firm's metal and molded closures will be maintained.

Clintwood Chemical Acquires New Plant

The Clintwood Chemical Company has acquired a new building with 25,000 square feet of space at 4324 South Wolcott Avenue, Chicago, for the manufacture of surfactants and fine chemicals for the cosmetic industry.

The firm plans to expand its products under the trade name Sandrol, and, in addition, to manufacture fine organic chemicals on a custom basis.

Shulton Acquires Hair Coloring Firm

Shulton, Inc., has acquired Tecnique, Inc., a midwest manufacturer and distributor of hair coloring products.

Sig Pass, who developed Tecnique Color-Tone, a hair color cosmetic, continues his present position, as president of Tecnique, Inc., subsidiary of Shulton.

The transaction was an outright cash purchase. The amount involved was not disclosed. The firm is to continue as formerly, amplified by the research, manufacturing, marketing, packaging, and sales facilities of Shulton.

Continental Oil Plans Petrochemical Plant

The Continental Oil Company plans to construct a multi-million dollar petrochemical plant at Lake Charles, La., for manufacturing from petroleum a line of alcohols formerly produced only from natural oils and fats.

The Conoco plant, the first of its type in the world, will have a capacity of more than 50,000,000 pounds annually of straight-chain primary alcohols, which will be marketed under the trademark Alfol, for use in the manufacture of detergents, plasticizers, cosmetics, lubricating oil additives, paper, textiles, and emulsifiers. Completion is scheduled for early in 1961.

American Home Products Buys New York Skyscraper

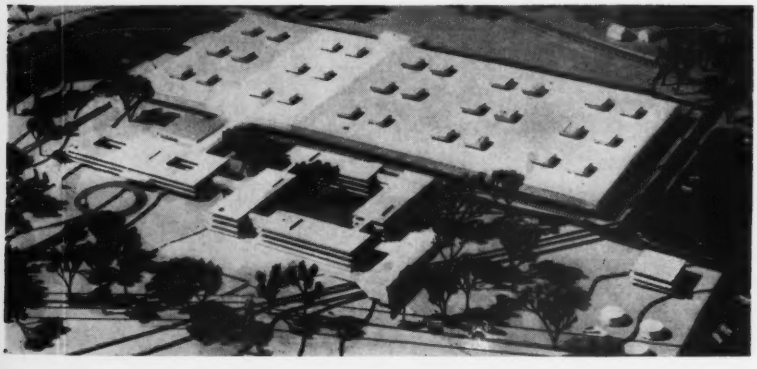
The American Home Products Corporation has taken a 40-year lease on a 25-story skyscraper being constructed at the northeast corner of Third Avenue and East 43rd Street, New York City. The 200,000 square feet of space at 685 Third Avenue will be occupied entirely by American Home Products, which will thus house all of its New York offices under one roof.

New Michigan Can Plant

The Continental Can Company plans to build a 250,000-square foot can plant and warehouse in Shoreham, Michigan, a suburb of St. Joseph.

Initially equipped to produce 250 million cans a year, the plant is designed for expansion to nearly double that capacity, and to include lacquer coating and end-fabricating equipment.

Architect's model of the new multi-million dollar plant of McNeil Laboratories, Inc. on 89-acre site in Philadelphia suburb. White section, to be ready in the Fall, 1960, will house 450 persons initially, twice McNeil's present home staff, for research, manufacturing, administration.



Alexander R. M. Boyle

Alexander Robert Mills Boyle died September 10 in Darien, Conn., of a heart condition.

A. R. M. BOYLE

Mr. Boyle, treasurer and a director of Lehn & Fink Products Corporation for 32 years, had retired in 1957, but continued as a director and consultant on fiscal matters. He was 71 years old.

Stone Container Buys Acme Carton

Stone Container Corporation has bought the business of Acme Carton Company, Chicago manufacturer of folding cartons and set-up boxes. The operation is to continue as Acme Carton Division of Stone.

Lee Bernstein, Acme's president, is now in charge of the division as general manager. No personnel changes are planned.

Acme becomes the third package manufacturing division in Chicago for Stone Container, whose total operations include four container plants, five carton plants, and three paperboard mills.

National Can Builds Second Washington Plant

The National Can Corporation has announced its second plant in the State of Washington, this one at Yakima. Production capacity for the 60,000-square-foot installation will be a million cans annually. It is to be built along the Northern Pacific Railroad, on a ten-acre site that includes room for expansion.

The company has already announced its agreement with the Port of Vancouver for a plant which will provide certain services to the contemplated Yakima plant, as well as producing more than 150 million cans a year for the Vancouver area.

(*Continued from page 491*)

ment filled with spys, an industrial environment in which the true scientist would be embarrassed to participate because he could not talk freely of what he knew, and he could not use freely what he had learned."

With regard to small companies and new companies Dr. Land's position is: "It is impossible for a new company involving a major advance in science or technology—first, to be properly financed; second, to go through the extremely difficult periods of study, invention, development, engineering, and production; third, to afford to advertise and to afford to distribute—all this is impossible—without protection by patents."

Rise V. Rapid Shave

According to a recent federal court opinion, it would appear that Colgate-Palmolive has won an important victory against Carter Products, the fourth circuit court of appeals affirming a lower court's decision holding the Spitzer patent is not infringed by Colgate Rapid Shave which employs isobutane and propane hydrocarbons in place of Freons.

It is felt that the readers of this journal are fully familiar with the background and extensive litigation between the parties involving U. S. Patent 2,655,480 issued to Spitzer et al. on pressurized shaving cream. Carter Products is the exclusive licensee under that patent whose validity was sustained against Colgate, which had also been held to infringe.

It will be recalled that after Colgate modified the composition of its shaving cream by substituting hydrocarbons for Freons, Carter asked the courts to rule that that substitution did not avoid the patent.

Since the patent claims cover only Freon propellants, Carter did not contend that the use of the saturated aliphatic hydrocarbons *literally* infringed the patent claims but, rather, Carter claimed that the hydrocarbons are the *equivalents* of the Freons.

The lower court agreed with Carter that the hydrocarbons were the equivalents of the Freons but ruled that since reference to such hydrocarbons had been deleted from the original claims "to escape rejection upon reference from the prior art," Carter could not recover here by invoking the so-called doctrine of equivalents anything it had given up to meet the Examiner's objection based upon the prior art.

Without going into the legal technicalities raised by Carter on the appeal, it is believed sufficient to say for our purposes that the Court of Appeals refused to upset the lower court's ruling.

Nothing is known by the writer concerning the plans of Carter with respect to any further litigation on this point. However, it is noted that there always is the possibility of asking the U. S. Supreme Court to review a decision of a federal Court of Appeals, as well as the possibility of patent litigation on the same point in another circuit.

RECENT PATENTS

2,894,949—Wm. S. Merrell Co.—Oxa Azabicyclo Derivatives.

2,894,952—Wm. S. Merrell Co.—Indenones.

2,894,955—Upjohn—Pyrrolidine-Butyronitrile.

2,894,958—Hoffmann-La Roche—Acetyl Oxo Dodecahydrophenanthrene.

2,894,960—Les. Labs. Fr. de Chim. (France)—Succinoxy Hydroxy Keto Cholenic Acid.

2,894,961—G. D. Searle—Arylhydrazones of Trihydroxy Pregnen-One.

2,894,963—Schering—Dihalogeno Pregnenes.

2,894,964—Ethicon—Diketo Hydroxystearic Acid.

2,894,965—American Cyanamid—Octanoic Acid Esters.

2,894,972—Chas. Pfizer—Isonicotinylhydrazino Alkanoic Amides.

2,894,987—Merck—Allyl Aminoisocamphane.

2,895,871—Diamond Alkali—Polychlorobenzhydrols.

2,895,874—Whitmoyer Labs.—Diamino Pyrimidine as Anti-Coccidiosis.

2,895,875—H. Klette—Subcutaneous Hormone Pellets.

2,895,876—Chas. Pfizer—Catenulin.

2,895,877—McNeil Labs.—Spasticity-Relieving Composition.

2,895,878—Eastman Kodak—Stabilized Vitamin A-Containing Compositions.

2,895,879—Eastman Kodak—Gelled Glycerol Fatty Acid Partial Ester.

2,895,880—Smith, Kline and French, Labs.—Sustained Release Pharmaceutical Product.

2,895,881—Wynn Pharmacal Corp.—Quinidine Gluconate Sustained Medication Tablet.

2,895,954—Olin Mathieson—Steroids.

2,895,957—Upjohn — Dimethyl Piperidine Diphenyl Butyramides.

2,895,968—Merck—Bisnorcholadienic Acids.

2,895,969—Syntex—Cyclopentanophenanthrenes.

2,895,970—Chas. Pfizer—Bisnorallo Cholenaldehydes.

2,895,988—Sterling Drug — Acylated Triiodo-Aminophenylalkanoic Acids.

2,895,993—Chas. Pfizer — Alkyl Substituted Anhydrotetracycline.

2,897,116—Burroughs Wellcome—Dihydrotriazines with Anthelmintic Properties.

2,897,118—Merck—Stable Vitamin A Compositions.

2,897,120—Upjohn—Low Viscosity CMC Pharmaceutical Vehicle.

2,897,119—Van Camp Sea Food Co.—Stable Powdered Oil Soluble Vitamins.

2,897,121—Upjohn—Enteric Product.

2,897,122—Charles E. Frosst and Company—Enteric Coated Product.

2,897,128—Chas. Pfizer—Steroids.

2,897,196—G. D. Searle—Epidithiopregnanes.

2,897,198—Upjohn—Alkene Hydroxy Pregnanes. •

New uses
are still being found for

GROCO RED OILS & WHITE OLEINES

SPECIFICATION	WHITE OLEINES		RED OILS			
	GROCO 6 USP	GROCO 5L Low Linoleic	GROCO 2	GROCO 4	GROCO 8	GROCO 18
Titre	2° – 5°C.	2° – 5°C.	3°C. max.	4° – 6°C.	8° – 10°C.	18° – 20°C.
Titre	36° – 41°F.	36° – 41°F.	37.4°F. max.	39.2°–42.8°F.	46.4°–50.0°F.	64.4° – 68°F.
Color 5¼" * Lovibond Red	1 max.	1 max.	1 max.	1 max.	1 max.	2 max.
Color 5¼" * Lovibond Yellow	8 max.	8 max.	10 max.	10 max.	10 max.	15 max.
Color Gardner 1933	2 max.	2 max.	—	—	—	—
Unsaponifiable	1.0% max.	1.0% max.	1.5% max.	1.5% max.	1.5% max.	1.5% max.
Saponification Value	199 – 204	201 – 206	198 – 203	198 – 203	198 – 203	204 max.
Acid Value	198 – 203	200 – 205	197 – 202	197 – 202	197 – 202	203 max.
% F.F.A. as Oleic Acid	99.5 min.	99.5 min.	99 min.	99 min.	99 min.	99 min.
Iodine Value (WIJS)	95 max.	90 max.	95 max.	94 max.	92 max.	85 max.
Refractive Index 50°C. (Average)	1.4500	—	1.4505	1.4500	1.4495	1.4485
Total Polyunsaturated Fatty Acids	—	3.5% max.	—	—	—	—
COMPONENT FATTY ACIDS						
C14 Myristic	5%	6%	5%	5%	5%	5%
C16 Palmitic	3%	2%	4%	5%	6%	10%
C18 Stearic	1%	—	1%	1%	2%	4%
C18 Oleic	82%	89%	80%	79%	77%	72%
C18 Linoleic	8%	2.5%	9%	9%	9%	8%
C18 Linolenic	1%	0.5%	1%	1%	1%	1%
MACKEY TEST: Time to reach 105°C.	over 7 hrs.	over 7 hrs.	over 4 hrs.	over 4 hrs.	over 4 hrs.	over 3 hrs.

For more information on A. Gross fatty acids, send for new edition of "Fatty Acids in Modern Industry."

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COMING EVENTS . . . . .

OCTOBER

16 **National Vitamin Foundation,** symposium on the role of vitamins and other nutrients in lipid metabolism, Auditorium, Tulane University School of Medicine, New Orleans, La. (N.V.F., 149 E. 78th St., N. Y. C. 21)

(Continued on page 418)

17-25 **International Fair of the Plastics Industry** (for producers, processors, machinery manufacturers), Dusseldorf, Germany (German-American Chamber of Commerce, Inc., 350 Fifth Ave., N. Y. C. 1)

19-23 **National Safety Council,** national congress ad exposition, Chicago, Ill. (R. L. Forney, N.S.C., 425 N. Michigan Ave., Chicago 11, Ill.)

19-23 **American Public Health Assn.,** annual meeting, Convention Hall, Atlantic City, N. J.

20-21 **Pharmaceutical Manufacturers Assn.,** Pharmaceutical Contact Section, Washington Hotel, Washington, D.C. (Dr. Karl Bambach, P.M.A., 1411 K Street, N.W., Washington 5, D.C.)

22-23 **Pharmaceutical Manufacturers Assn.,** Production and Engineering Section, Van Cleve Hotel, Dayton, Ohio (See above.)

25-28 **National Flexible Packaging Assn.,** fall meeting, White Sulphur Springs, West Virginia)

25-28 **Pharmaceutical Manufacturers Assn.,** Financial Section, Greenbrier Hotel, White Sulphur Springs, W. Va. (See above.)

NOVEMBER

1-5 **German Society of Cosmetic Chemists,** scientific and cosmetic sessions, Baden-Baden, Germany (Dr. Herbert Neugebauer, Baden-Baden, Metzgerstrasse 30, Germany)

2-4 **American Management Assn.,** seminar on manufacturing's part in the packaging program, Hotel Astor, N.Y.C. (A.M.A., 1515 Broadway, N.Y.C. 36)

2-4 **American Management Assn.,** seminar on printing on packaging, Hotel Astor, N.Y.C. (See above.)

2-4 **Pharmaceutical Manufacturers Assn.,** Research and Development Section, Greenbrier Hotel, White Sulphur Springs, W. Va. (Dr. Karl Bambach, P.M.A., 1411 K Street, N.W., Washington 5, D.C.)

3 **1959 Exposition of Chemical Industry,** Coliseum, N. Y. C. (through December 4)

3-5 **Packaging Assn. of Canada,** national packaging exposition, Automotive Building, Exhibition Grounds, Toronto, Canada

4-6 **Symposium on Antibiotics,** Mayflower Hotel, Washington, D. C. (Dr. Henry Welch, Director, Div. of Antibiotics, F. D. A., U. S. Dept. Health, Education, and Welfare, Washington 25, D. C.)

7-12 **National Wholesale Druggists' Assn.,** annual convention, Americana Hotel, Bal Harbour, Fla. (Harry A. Kimbriel, N.W.D.A., 60 East 42nd St., N. Y. C. 17)

9-11 **American Management Assn.,** seminar on fundamentals of packaging specifications, Hotel Astor, N.Y.C. (See above.)

9-12 **Glass Container Manufacturers Institute,** semi-annual meeting, Arizona-Biltmore Hotel, Phoenix, Arizona (H. W. Kuni, 99 Park Ave., N. Y. C. 6)

12-14 **Gerontological Society,** Statler Hotel, Detroit (Administrative Secretary, Mrs. Marjorie Adler, 660 S. Kingshighway Blvd., St. Louis 10, Mo.)

16-18 **Packaging Institute,** annual national packaging forum, Hotel Statler, N. Y. C. (Charles A. Feld, P.I., 342 Madison Ave., N. Y. C. 17)

16-20 **Fifth International Automation Congress and Exposition,** New York Trade Show Bldg., New York City.

17-20 **Packaging Machinery Manufacturers Institute Show,** New York Coliseum, N. Y. C. (Albert R. Stevens, Elgin Mfg. Co., Inc., Elgin, Ill.)

24 **Manufacturing Chemists' Assn.,** Statler Hilton Hotel, New York City (M. F. Crass, M.C.A., 1825 Connecticut Ave., N.W., Washington 9, D. C.)

30 **Exposition of the Chemical Industries,** New York Coliseum (E. K. Stevens, International Exposition Co., 480 Lexington Ave., N.Y.C. 17)

DECEMBER

1 **Toilet Goods Assn.,** scientific section, winter meeting, Waldorf-Astoria Hotel, N. Y. C. (Kathryn Fitzpatrick, Americas Bldg., Rockefeller Center, N. Y. C. 20)

2 **Synthetic Organic Chemical Manufacturers Assn.,** annual meeting and dinner, Hotel Roosevelt, New York City (S. Stewart Graff, Sec., S.O.C.M.A., 41 East 42nd St., N. Y. C. 17).

7-9 **Pharmaceutical Manufacturers Assn.,** mid-year and eastern regional meeting, Waldorf-Astoria Hotel, N. Y. C. (Dr. J. O'Neill Closs, P.M.A., 1411 K Street, N.W., Washington 5, D.C.)

7-9 **Chemical Specialties Manufacturers Assn.,** annual meeting and aerosol package contest, Mayflower Hotel, Washington, D.C. (C.S.M.A., 50 E. 41st St., N.Y.C. 17)

7-10 **American Medical Assn.,** clinical meeting, Dallas Auditorium, Dallas, Texas

9 **The Proprietary Assn.,** Research and Scientific Development meeting, Hotel Roosevelt, New York City (Dr. Howard A. Prentice, 810 18th St., N.W., Washington 6, D.C.)

1960

JANUARY

9 **Northwest Society for Clinical Research,** Seattle, Washington (Dr. John R. Hogness, 721 Minor Ave., Seattle 4, Wash.)

11-13 **American Academy of Allergy,** Hollywood Beach Hotel, Hollywood Fla. (James O. Kelley, 756 N. Milwaukee St., Milwaukee 2, Wisc.)

FEBRUARY

3-5 **Pharmaceutical Manufacturers Assn.,** Legislative Section, Boca Raton, Fla. (Dr. Karl Bambach, P.M.A., 1411 K Street, N.W., Washington 5, D.C.)

8-10 **Pharmaceutical Manufacturers Assn.,** central regional meeting, Edgewater Beach Hotel, Chicago, Ill. (Dr. J. O'Neill Closs, 1411 K Street, N.W., Washington 5, D.C.)

15-16 **Pharmaceutical Manufacturers Assn.,** western regional meeting, Ambassador Hotel, Los Angeles, Calif. (Dr. J. O'Neill Closs—see above.)

25-27 **Symposium on Fundamental Cancer Research,** Univ. of Texas, Houston, Texas (Univ. of Texas, M.D. Anderson Hospital and Tumor Institute, Houston 5, Texas)

28 **American College of Allergists** (through March 5) Americana Hotel, Bal Harbour, Miami Beach, Fla. (Eloi Bauers, 2160 Rand Tower, Minneapolis 2, Minn.)

MARCH

2-4 **Pharmaceutical Manufacturers Assn.,** Medical Section, Hollywood Beach Hotel, Hollywood Fla. (Dr. Karl Bambach—see above.)

3 **Drug, Chemical and Allied Trades Association, New York Board of Trade, Inc.,** annual dinner (Helen L. Booth, D.C.A.T., 291 Broadway, N. Y. C.) ●

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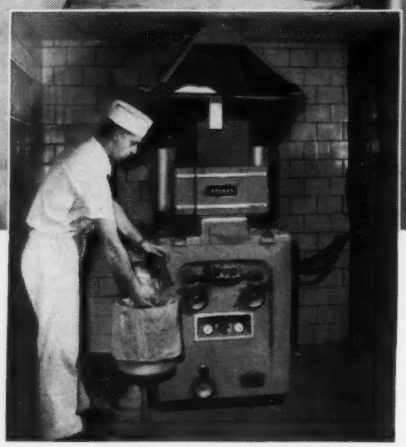
Stokes Model 533 tabletting machine is used for slugging material for Kolantyl tablets. It has reduced processing time by one day per batch.



Stokes Model 540 tabletting machine gives approximately twice the old production rate. It's used at Merrell for compressing several types of tablets.

at the Wm. S. Merrell Company...

Stokes presses speed production, keep costs down

For 131 years, the Wm. S. Merrell Co. of Cincinnati has been producing ethical pharmaceuticals for outlets on six continents. Recently, the company raised production substantially with Stokes high-speed rotary tabletting machines.

Stokes Model 533, for example, is used at Merrell in slugging material for Kolantyl tablets —an antacid which gives immediate acid neutralization as well as long-time antacid effects. The new Stokes press operates at three times the old rate. Its harder and more uniform slugs result in a more uniform final product—in hardness, dimension and disintegration rate. Rejects have been virtually eliminated. And the 533 reduces processing time at Merrell by one day per batch! Controls on the Stokes 533 are operator-oriented and all moving parts are adequately shielded. What's more, the machine requires only ⅔'s the floor space of former equipment.

When you need high-speed tabletting machines, talk to your nearby Stokes representatives. They'll be glad to show you how you *can* have equipment quality plus economical operation. And Stokes Advisory Service will help you plan production, select equipment and train personnel. Why not look into it further . . . today.

Pharmaceutical Equipment Division
F. J. STOKES CORPORATION
5500 Tabor Road, Philadelphia 20, Pa.

STOKES

Management Forum

BY FRANCIS CHILSON
INDUSTRIAL CONSULTANT

The Chilsonator

From time to time I have commented on the progress of the Chilsonator, which was invented by yours truly and is now being made available to the trade by The W. J. Fitzpatrick Company, 1001 Washington Boulevard, Chicago 7, Ill. I invented this machine several years ago and for many of these years it has been in successful operation in the plant of the Chatanooga Medicine Company. (It now is in successful operation in many other plants as well.) The Chilsonator is intended to eliminate wet granulation for most if not all products and it is designed to simplify and speed up the process of making dry granulations usually known as "the slugging process." One of Fitzpatrick's customers reported that one Chilsonator would do the work of four slugging presses on his product. The cost of the machine is about the same as a slugging press.

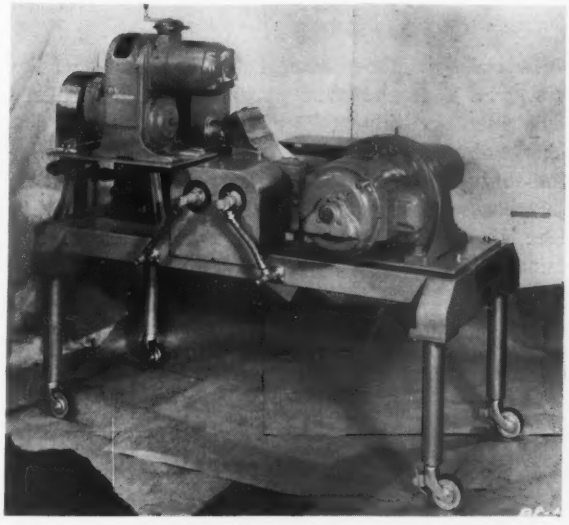
After taking over the patent rights Fitzpatrick redesigned the machine. It now has hydraulically controlled rolls which are cored for the circulation of hot water or refrigerants as needed, and also means of controlling the feed to the rolls.

The machine consists of a pair of specially grooved rolls which rotate toward each other. The material to be granulated is fed to these rolls at a controlled rate and the pressure between the nips of the rolls also is regulated by hydraulic means. Pressure up to 100,000 psi can be exerted if required. This is several times the pressure that can be exerted between the punches of a slugging press. Materials that normally have to be slugged two or three times can be granulated in a single pass through the Chilsonator.

In operation, the material of the batch is given a dry mix. If it contains color or minute quantities of ingredients that are difficult to disperse, it is good practice to run the batch through a regular Fitzmill to get proper dispersion before the material is granulated. In regard to some materials a small percentage of alcohol or water added may prove helpful as a starter. The heat of compression from the rolls will in any case remove it. The mixed material is then fed to the Chilsonator and the compressed granules or strips will be discharged in irregular length pieces ranging from an eighth to an inch long. It is of course necessary to run the product of the Chilsonator through a dry granulator or Fitzmill to secure the proper size granulation from which to make the finished tablets. Thus the Chilsonator does away with wet mixing, wet granulating, tray spreading and drying. Density of granulation is regulated by adjusting the pressure between the rolls.

Heavy chemical manufacturers are showing a keen interest in the machine as a means of pelletizing fine mesh chemicals which are subject to considerable dusting loss during handling and transit. Feed manu-

The Chilsonator.



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The Colletta bench-type labeling unit is the ideal solution to short run labeling problems.

Basically a semi-automatic, hand-fed unit, it is readily converted to an automatic machine by use of auxiliary attachments providing fully mechanized intake and discharge of objects being labeled. Labels are applied with full-surface glue adhesion to a range of shapes in bottles, jars, boxes, books, etc. up to diameter or height of 5½". Size changes are made within a maximum of five minutes.

Designed and manufactured by Jagenberg of Dusseldorf, this Universal Labeler is now sold exclusively in the United States by Pneumatic. Write for Bulletin 138 which provides detailed information. Better still, send in samples of objects presenting production labeling problems at your plant. A prompt analysis and quotation will be submitted.

PNEUMATIC SCALE CORPORATION, LTD. 70 Newport Avenue, Quincy 71, Mass. *Sales Offices: New York; Chicago; Dallas; Rochester. Agents: Fred Todt Company at Los Angeles, San Francisco and Seattle; Rockwell Pneumatic Scale Ltd., Edgware Road, London, N.W. 2, England; O.R.M.A., Paris 8, France. Subsidiaries: Delamere & Williams Co., Ltd., Toronto; Carbert Manufacturing Co., Inc., Cambridge, Mass.*

★PNEUMATIC

Packaging and Bottling Equipment

Visit BOOTH 307, PMMI SHOW, New York Coliseum, Nov. 17-20, 1950

facturers likewise are showing a keen interest in the machine as a means of granulating feeds to prevent feeding losses on farms.

Padding the Payrolls

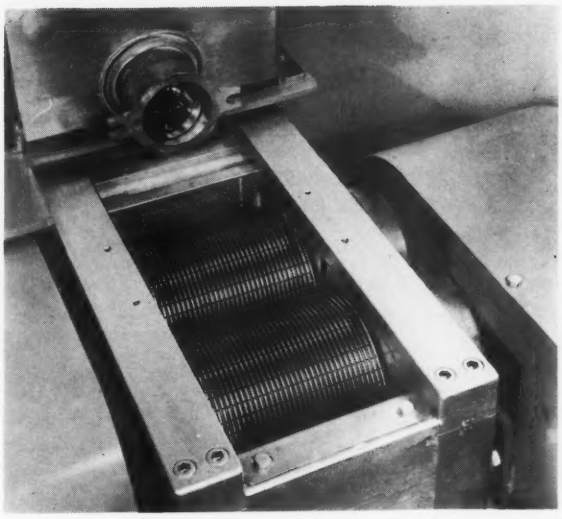
It used to be only the bookkeepers who were routinely accused of padding the payrolls, but as I pointed out in this column a few months ago, the practice has been adopted and legalized by big shots, who fatten their purses by all manner of stock option plans, percentage compensation plans, bloated pension plans, deferred earnings plans, and other gimmicks which cheat the stockholders. Now Kiplinger has taken notice of such nefarious practices and in his September fifth letter has this to say:

"High-salaried executives in many companies are under suspicion by their stockholders for feathering their own nests too liberally.

"It's a minor rebellion against the many schemes for extra pay that company officials urge for themselves . . . stock options, big pensions, compensation deferred until after retirement, other forms of incentives. Usually the companies tell stockholders that such schemes are necessary to get and keep top quality executives . . . that it's cheap at the price. But stockholders are starting to wonder whether things have gone too far, whether their own holdings are being diluted, and whether top executives aren't a trifle 'grabby' . . . at the expense of company AND stockholders."

Mechanical Cow

The British have done it again. According to the N. Y. Times of Sept. 11th, a firm known as British Glues and Chemicals has invented a mechanical device which will convert into edible protein almost any vegetable substance fed into it. The pilot plant produces about a ton an hour of a dry powder having no odor or taste. Seven years were required to perfect the apparatus with a total investment of only $84,000.00. The machine works by breaking down vegetable cells by shock waves transmitted through a mildly alkaline menstruum. Insoluble carbohydrates, fibre, oil and protein are separated. Sounds like too big an order for one machine to accomplish by so simple a means. Newspaper reporting of technical matters is generally sketchy or inaccurate. (Don't write and ask for the address of the company; I don't have it.) The thing that intrigued me about this process was the use of electrolysis in an extraction mechanism. Before the trade lost interest in the extraction of botanical drugs I did a lot of work on this subject and I had a repeated hunch that the application of electrolysis to an extraction vessel might yield some valuable products other than the ones we were extracting by conventional means. I also thought of appyling ultrasonic vibration and sound waves. But I never got the chance to fool around with any of these ideas because my clients and the trade in general lost interest in botanical extraction. Parenthetically, I've noticed that interest is being renewed in the subject and I may once again have a chance to fool around in an interesting field. This trade has been notoriously niggardly in spending money for engineering research. It has been only within the last four or five years that any firm has been willing to gamble the money required to develop new processes and equipment.



Open view of the Chilsonator showing specially shaped grooves.

Engineering Research

The pharmaceutical industry spends millions of dollars annually on research in the chemical sciences and hardly a dollar on engineering research. Apparently no one realizes that, as by-products, engineering research could yield new dosage forms and even new products or packages. About the only engineering research and development for this trade has been done by a few equipment manufacturers interested in the pharmaceutical industry. Manufacturers are content to use equipment developed principally for other industries. Every engineer and production man in this industry is always asked before he is allowed to purchase even a piece of standard equipment: "Are you sure it will work?" If the answer is affirmative and the purchased machine doesn't work, what a hell of a row is kicked up! Yet the same president, who kicks up a hell of a storm about the failure of a $20,000.00 investment in equipment, will not batt an eyelid at the failure of a quarter million dollar investment in an abortive research or advertising program. Such losses are accepted as part of the chances that must be taken. This attitude is especially noticeable in the proprietary side of the business. One big company president told me he regarded production as a necessary "damn nuisance." Another told me that production equipment was "all Greek" to him and if he had his way he'd quit manufacturing and get rid of "the headache" by turning produc-

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tion over to Strong Cobb (Now Strong Cobb Arner).

These are extreme cases of course. It is a fact however that no firm in this industry has set up a large scale engineering research program to evaluate all its processes and equipment. One cannot expect small manufacturers to do this except in concert with others. Smaller firms however can benefit by making a critical analysis of equipment developed for unrelated industries. As a matter of fact I have taken considerable pride in introducing to the drug and cosmetic industries processes and equipment developed by and for unrelated industries. I think this approach was the right one when our industries were relatively small. I think it is still the right approach to take in initiating an engineering research project even if for no other reason than to establish a comparative standard of efficiency. But if a machine developed for another industry, and perhaps for an entirely dissimilar process, can be used directly or adapted to the purposes of the engineering research project, it may provide an adequate solution or it may provide a proven starting point.

Beginning with the introduction in 1927 of the high-speed pulverizer as a means of making face powder and the introduction of the Pittsburgh Lectrodryer about 1930 as a means of drying air, I could recite a long list of introductions I have made—usually against considerable resistance I may add—but the most striking example of trade lethargy in regard to process improvement was my failure to arouse interest in press coating and tablet printing during the Thirties. In 1932 I produced experimentally for Grove Laboratories both press-coated tablets and imprinted tablets. For marketing reasons the company decided not to adopt either for Groves Bromo Quinine tablets. When the company decided not to utilize either of these new ideas, I wrote an article about them in this magazine about 1933. There wasn't a whisper of interest in the trade. I repeated the articles in 1940 or '41. Still no interest. Suddenly after the war everybody became interested both in press coating and in tablet printing!

I do not insist that we should try to revolutionize every process and every piece of equipment because usage, potential economies and other factors indicate where research engineering money can best be spent. But I think that every process and every piece of equipment should be analyzed with a critical eye on the assumption that improvements can always be made even upon the most perfect of installations.

Fuel Cell

In England a chap named Francis Bacon (smart enough to be a descendant of the original—assuming he isn't), demonstrated at Cambridge University a revolutionary new electric cell with a conventional lift truck. The cell consists of a series of porus nickel plates separated by a solution of potassium hydroxide. When oxygen is fed into the individual cells the contact between nickel and oxygen produces charged oxygen atoms—ions—which migrate across the filled cells to recombine with the hydrogen being fed in at the opposite side. This results in a difference in electrical potential amounting to forty volts in the whole series of individual cells. On test the cell delivered about 7½ horsepower. It weighs about 800 pounds loaded. Unlike batteries such cells do not have to be repetitively recharged. Such cells of proper size might someday be used to power ships and trains that now use coal or oil. It would be a godsend to have lift trucks that didn't have to be recharged every day or twice a day, depending upon size and usage, like the present electric trucks, or didn't stink or pollute the air with carbon monoxide like the gas driven trucks.

Diagnosis Machine

Some time ago I described in this column Chilson's Diagnostic Slot Machine which would determine what ails you by electronic means. All you had to do was, drop quarters in the appropriate slots. This machine was to have eliminated the guesswork done by doctors—professionally known as "diagnosis." Y'all thought I was spoofing but I was actually foretelling the future. System Development Corp. in Santa Monica, California has developed a diagnostic machine along the lines I envisioned. As in my projection, this machine provides buttons which the patient can push to record his symptoms. Blood and urine analyses are made automatically. The machine analyzes the symptoms and tests and comes up with an answer for the doctor. According to the description in *Time*, "The cybernetic brain compares the patient's symptoms with those of diseases it has previously learned, discards all but three, and offers these to the doctor by code number." My machine was more accurate. It gave the doctor no choice at all for the reason that if a doctor is given three choices you can always depend upon him to pick the wrong one.

British Brains

I have always maintained that the British are first-rate, fundamental thinkers. This opinion was proved by the results of a poll conducted by the University of Bridgeport. The university asked 1,116 distinguished scientists in fifty countries to vote for the scientists who had made the most important discoveries not based upon previously known laws of nature. The candidates for election must have been dead at least ten years. When the votes were tabulated it was found that not one was American or Russian. Eight were English, five German, four from ancient Greece (as one would expect) and the rest were from France, Italy, Poland and Czechoslovakia. The English can well be proud of a contribution like this.

We may however catch up. Basic research in this country has been accelerating and broadening since World War II. Using the Nobel prizes as an indicator

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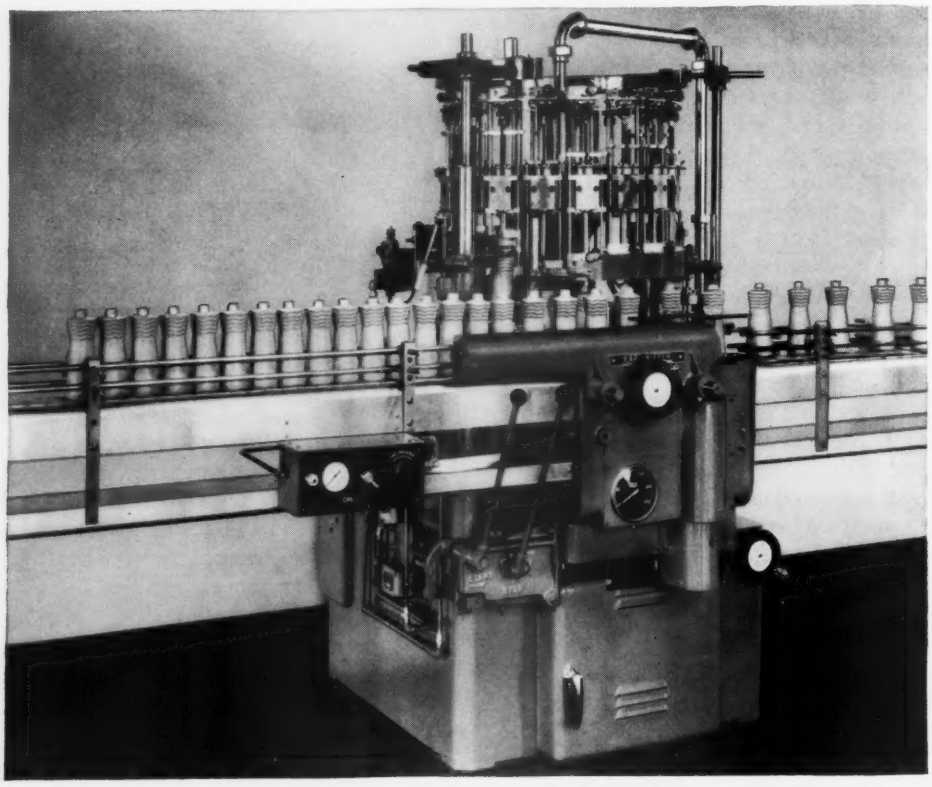

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the score to date is as follows:
Physics: U.S. 8; Russia 3; all others 11.
Chemistry: U.S. 8; Russia 1; all others 8.
Medicine & Physiology: U.S. 16; Russia 0; all others 9.

I was a Juvenile Delinquent

In the press these days there is a continuing uproar about juvenile delinquency as if this state of affairs is a recent phenomenon. I think the uproar exaggerated, because all active boys pass through a phase of juvenile delinquency. (But you stuffed shirts will not admit it now.) I was a thief myself at seven years of age. I once stole a bright new express wagon from another little boy by the simple process of punching him in the nose and taking it away from him. I brought it home and concealed it to avoid the possibility of senseless questions on the part of the hostile paternal division. By some means or other my old man learned about my new acquisition and he made me dance a horn-pipe with my collar in one hand and his razor strop in the other. (The invention of the safety razor probably had a lot to do with the increase in juvenile delinquency.) Adding insult to injury, he made me take the fruits of my enterprise back but, unfortunately, the father of the little boy from whom I had stolen the wagon caught me as I was making restitution, and he too larruped the hell out of me. Thus early I was made familiar with double jeopardy. Clearly this second trouncing was a violation of my constitutional rights. My backside still hurts when I think of it. My career as a thief was not only nipped in the bud; it was smacked out on the bottom.

The Nose Knows

Automation has begun to creep into the perfumer's hitherto sacrosanct bailiwick. At a meeting at the University of Michigan, Dr. D. A. M. Mackay of Evans Research reported a machine developed initially in England that can detect and analyze odors and flavors. The machine consists of a series of ionization detectors attached to gas chromatographs. Vapor from a sample to be analyzed is fed into a column which indicates the several components of which it is composed. This I gotta see!

The Architects

People accuse me of hating architects. They say I am blindly prejudiced against them. This is nonsense. The fact is that two of my most intimate friends are architects—good ones. Everyone has prejudices, of course. I try to keep mine to a minimum and I am diligent about not allowing them to obtrude into my work. That would be disastrous. I don't hate anybody. But I do hate incompetence wherever it is exhibited, be it in engineering, architecture, law, medicine, or accounting. Professional men have no moral right to be incompetent. Professional incompetence is seldom caused by inadequate training, but by laziness, lack of thoroughness, indifference, inattention, and lack of specific experience, lack of imagination.

The sort of thing that makes my bile boil in respect to incompetence in architects was reported recently by *Time*, as follows:

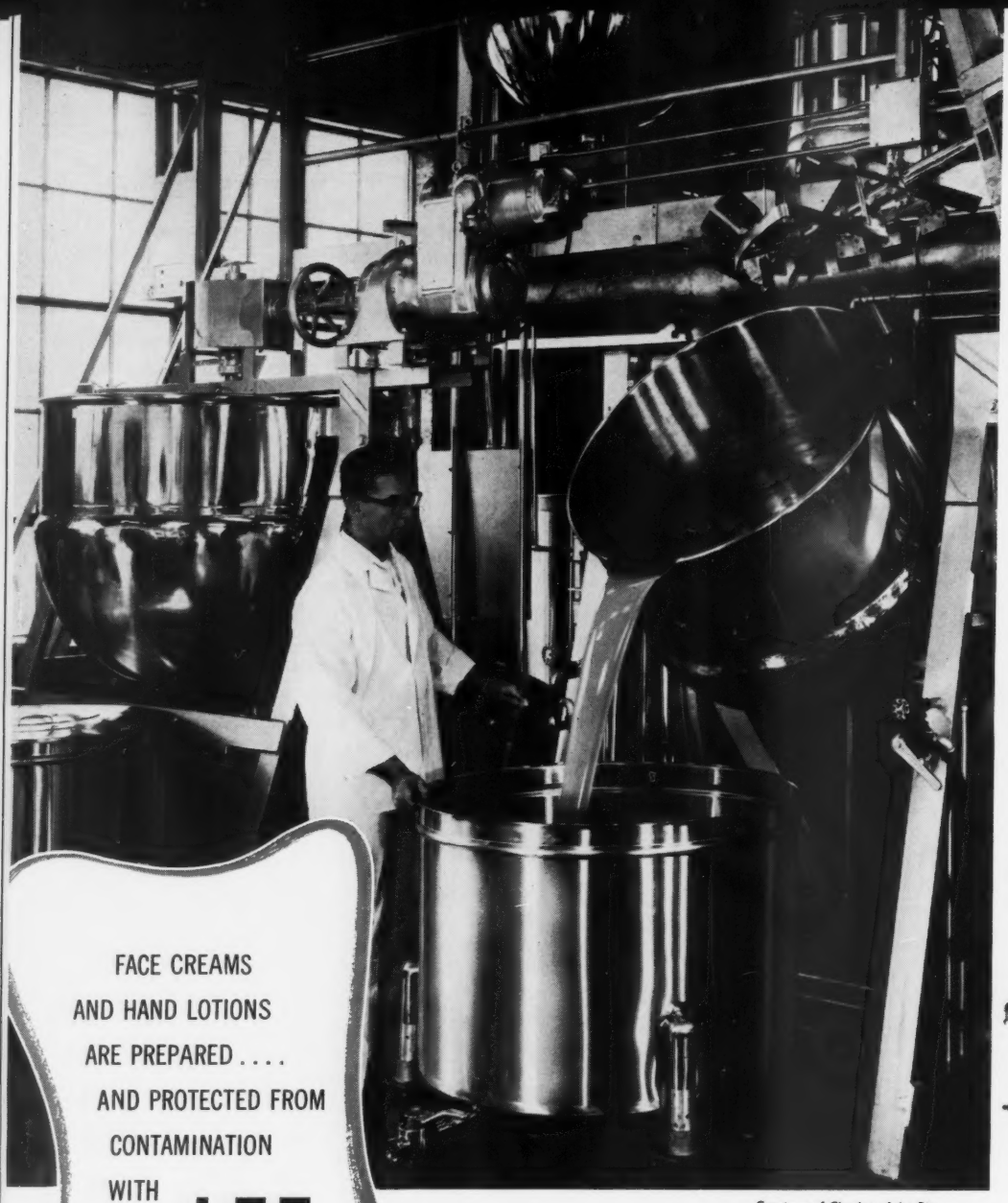
"Its grey-veined marble flanks as bleached as a great prehistoric bone, its entrance guarded by pretentious bronze doors, the new 500-room, $25 million Senate Office Building sprawled resplendently last week on Capitol Hill—dubbed 'The Great White Goof.'

"For all the money it cost, the proud new S.O.B. more vexatious than a slippery collar button. The clocks had bronze hands that were too heavy to hold the time. The mail chutes choked up with letters, had to be taped closed. Slow-moving elevators forced Senators to overflow into freight lifts. Private conversations were being filtered into the corridors through louvered air ducts in the doors. Long-legged lawmakers cracked their kneecaps against low-slung desks. And the new subway to the Capitol lay dead-ended about 250 ft. short of its destination (cost to complete: $4,000,000)."

And it is not so many years ago that a firm of architects designed an office building in Washington and forgot to include elevators. Such incompetence is inexcusable.

Medical Communism

Leaders of the pharmaceutical industry are "viewing with concern" the activities of the Russian and Chinese communists in exporting to underdeveloped and neutralist countries, all manner of drugs, particularly antibiotics, and medical services as well. According to reports from various sources which were published in the August fifth issue of the *Wall Street Journal*, the Russians now have a total trained medical personnel complement of 2,750,000 persons, an excessive number for their own requirements. They pirate American processes and patents and sell pirated products (which nevertheless are of excellent quality) at a fraction of U.S. prices. Along with this the Russians are offering to build pharmaceutical plants in underdeveloped countries. I foresaw this trend several years ago. As a matter of fact I wrote an article in this column a year or two ago speculating on the possibility that the Reds would use medicine and medical personnel to sell Communism to the backward nations. It seemed to me an obvious approach because the relief of illness makes a stronger appeal to individuals than the relief of hunger. Most of the backward nations are innured to hunger. It is endemic in most of them. It also seemed to me that the use of drugs and medical services is not only a relatively cheap means of political propaganda but an excellent means of economic and political penetration. For many years the U.S. through the Rockefeller Foundation and by other



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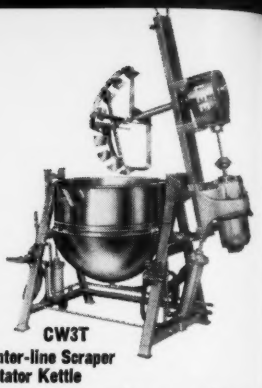
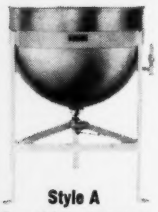
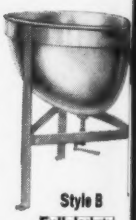


CW3T
Center-line Scraper Agitator Kettle
80 to 300 gal.

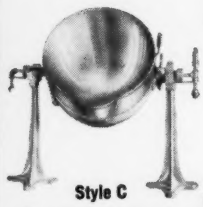
Quick Cooling Pan
50 to 200 gal.



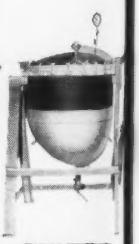
Style A
Two-thirds Jacketed
5 to 500 gal.



Style B
Full Jacketed
10 to 300 gal.



Style C
Two-thirds Jacketed
5 to 100 gal.

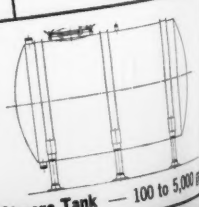


Pressure Kettle
Two-thirds Jacketed
40 to 200 gal.

Style CW
Two-thirds Jacketed
80 to 300 gal.

Pulp Tank
500 to 2,000 gal.

Mixing Tank
25 to
500 gal.



Storage Tank — 100 to 5,000 g

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means has done a notable job in disseminating medical assistance to poor nations; we have done a pretty good job in spots in disseminating public health practices but we never effectively coupled these activities with food production, which in the final analysis is the bed rock of public health. Even today government efforts to promote agricultural knowledge are not coordinated with public health activities. Both are parts of the same job.

New Colton Designs

The Arthur Colton Company, 3400 East Lafayette St., Detroit 7, Mich., has announced a new aerosol filling line of straight-line design, the Colton-Alpha, which handles up to 30 containers per minute. The line includes a variable speed drive; a double-ported, two-nozzle Model 15MS Colton-Hope filler; a single-head crimper, and a single-head pressure-filler, which eliminates the need for refrigeration.

The Colton Model 175 polyethylene tube sealing and conversion unit can be installed on Colton Model 17 or 175 filling machines. It fits in the place of the original folding and crimping heads for the metal tubes and can thus handle metal or plastic tube filling operations.

The new Colton-Hope rotary unscrambler operates in conjunction with a filling machine or other equipment, to handle a variety of containers with a speed matching the filling or packaging line.

Finally, the Kinsley Timing Screw accurately feeds round, oval, square, or rectangular glass bottles, metal cans, or plastic containers on a variety of the firm's packaging machines. Custom made for specific action, the device will pick up containers from a conveyor at random, move them under control acceleration and speed, and discharge them where required.

Wrapping and Bundling Machines

The Scandia Packaging Machinery Company, North Arlington, N. J., has developed an adjustable bundle collator attachment for the firm's Model 107 Automatic Wrapping and Bundling Machine, which automatically groups individual packages in collations of from 2 to 12 for multiple-wrapping or bundling. It handles up to 60 collations per minute.

The Model 609 High-Speed Automatic Wrapping & Multiple Wrapping Machine offers quick adjustability over a wide size-range of single packages, as well as multiple-pack collations.

Versatile Packager

The Hayssen Manufacturing Company, Sheboygan, Mich., has introduced its versatile RT machine, which interchangeably packages with polyethylene a variety of items.

The company's Model G Compak machine has a new automatic top-labeling attachment, which automatically applies a top label to the package as it is formed, filled and sealed.

Portable Mixing Equipment

A portable model has been added to its line of high-speed, high-shear mixing equipment by the Specialty Machinery Corporation, 50 Roanoke Ave., Newark 5, N. J. Model PM 756 accommodates batches of from 5 to 300 gallons, centers in a tank 48 in. in diameter requiring only 5 in. clearance underneath, and for smaller batches can straddle the container.

The mixer has spark-proof and solvent-proof plastic wheels and casters, and a snap-action floor lock which converts it into a fixed unit. It will handle a range of viscosities from water-thin to more than 100,000 cps., and is suitable for such diverse operations as tinting, making emulsions, premixing high solids, and grinding high-viscosity pastes.

Available in variable-speed and single-speed models, it has assorted blades and a quick-change system that permits exact selection of blade.

Magnetic Separator

A portable suspended plate magnet, complete with vibrating tray and secondary plate magnet, which is easily moved to various locations, has been introduced by The Magnetic Engineering and Manufacturing Company, 480 Van Houten Ave., Clifton, N. J. The Memco high power plate magnet is useful in removing tramp iron for the protection of grinding, pulverizing, and screening equipment, and purification of a given product.

Laboratory Ovens

The Despatch Oven Company, 619 S. E. 8th Street, Minneapolis, Minn., has designed a new oven, the Despatch Saf-T-Bilt, with improved shape and sizes for industrial laboratory use, more efficient direction of air flow in the work chamber, accurate temperature control throughout the work chamber, and new safety controls. Although electrically heated, it can be adapted to steam or hot water.

Safety features include an explosion relief panel, safety latches and chain, explosion-proof housing and motors, and strip heaters with welded connections to reduce spark hazards. It is available in sizes to fit any laboratory.

Heavy-Duty Dry Crusher

An improved heavy-duty dry crusher or pulverizer has been added to the dry grinding equipment manufactured by Charles Ross & Son Company, 148-156 Classon Ave., Brooklyn 5, N. Y. The #70-H size 4 Crusher incorporates a revolving crushing roll inside the hopper for preliminary breaking down of material. A handwheel adjusts clearance of plates and fineness of grind, which is then locked. Precise control of grind is insured by a guage, and variable speed drive makes it possible to get the best results with maximum production. Easily interchangeable plates make the machine versatile.

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Compounder's Corner

Anti-Static Comb and Brush

The paper by R. G. Barber and A. M. Posner in the July 1959 issue of the *Journal of the Society of Cosmetic Chemists*, "A method for studying the static electricity produced on hair by combing" brings back to my mind an idea I had several years ago and which still seems to be a good one. The idea, in brief, is to make or treat combs and brushes so that they will either prevent the development of a static charge on hair or immediately discharge it. Three approaches are possible: 1. If the comb or brush is grounded properly, the charge on the hair should leak away as it is formed; 2. A trace of radioactive substance would ionize the surrounding atmosphere and permit dissipation of the electrostatic charge; 3. Bristles of the brush or teeth of the comb could be coated or impregnated with a quaternary compound or similar anti-static agent.

The first approach involves the difficulty of creating conducting (metallic) teeth or bristles in a metal comb or brush and connecting these by means of a conductor to a good ground. The second approach could involve, as in some high fidelity record brushes, a small bit of polonium metal or other radioactive source to cause ionization of the air and permit the induced charge to escape from the hair. It should be possible to locate a radioactive material with emission characteristics that would not be harmful but would still do the job. With fall-out concern, radioactivity is not currently popular and this method of treating hair might involve difficult promotion. Finally, however, I see no reason why an anti-static substance cannot be incorporated in a plastic comb or plastic bristles, or used as a long-lasting coating. The static charge would then not develop on the hair, or would be immediately discharged. As a case in point, RCA Victor is now producing an anti-static phonograph disc containing ingredient "317 X" to make the discs permanently anti-static.

Emulsion Dosage Form

C. Riffkin and G. N. Cyr of the Squibb Institute for Medical Research described the oral emulsion formulation of a phenothiazine derivative to the August meeting of the Scientific Section of the A.Ph.A. in Cincinnati. With Vesprin, the burning taste and anesthesia in the mouth were overcome by incorporating the trifluprom azine base in corn oil as the internal phase of an emulsion. At a neutral *p*H, the concentration of the base in the aqueous phase is very low. The pharmacological action of the drug in this vehicle is the same as in standard dosage forms. The emulsion consisted of trifluprom azine 10.0; Tween 80, 10.0; Span 60, 10.0; Myrj 45, 10.0; butylated hydroxyanisole 0.5; butyl paraben 0.5; corn oil 500 ml.; sodium saccharine 5.0; sodium CMC medium viscosity 5.0; water to make 1,000 ml. and water-soluble preservative and flavor as required.

Hilfer's Patent

Harry Hilfer has been issued U. S. Patent 2,890,987, assigned to Witco Chemical Company, Inc., for "Stick-Form Astringent Compositions." This patent covers the use of a hot aqueous solution of a metallic astringent compound, a polyhydric alcohol, a solid fatty acid alkylolamide so that the final stick contains from 5 to 25 per cent of the astringent salt, 15 to 40 per cent of the polyhydric alcohol, 10 to 35 per cent of the alkylolamide, and from 10 to 40 per cent of water. The mixture forms a clear melt below 100°C. and may be cast into sticks which are white and opaque.

Sustained Action Liquid Suspension

The formula for a liquid suspension of methapyrilene adsorbed on an ion-exchange resin capable of permitting sustained release of the drug was presented by H. A. Smith, R. V. Evanson, and G. J. Sperandio to the Section on Practical Pharmacy of the 106th A.Ph.A. Convention, along with the testing procedures and results. The product was shown to possess pharmacological activity at least equal, if not superior, to a solution of methapyrilene hydrochloride and the results of this work indicate that a sustained release of methapyrilene taken orally may be accomplished by the use of sulfonic acid cation exchange resins, and that the rate of release may be controlled by the proper selection of the degree of cross-linkage and particle size of the resin.

Colloidal Silica

Cab-o-sil, offered by Godfrey L. Cabot, Inc., of Boston, is a silica prepared at high temperatures by the hydrolysis of a silicon compound; it is characterized by extremely small particle size. This particle size (enormous particle surface) leads to the application of Cab-o-sil as a thickening and gelling agent, suspending agent, thixotropic agent, to confer free-flowing characteristics, as an inert carrier, as a tablet ingredient, and as an oil adsorbent. The material is non-irritating and non-toxic and is acceptable for topical or oral use.

Cab-o-sil will produce soft gels with a wide variety of liquids, including water, butyl alcohol, turpentine and benzene; as little as 0.2 to 0.3 per cent will retard the settling of pigments in water or organic liquids. In mineral oil, 1 per cent will increase viscosity from 410 to 8,000 centipoises; it can be used to prevent caking in powders and keep them free-flowing. Suggested applications include use as a free-flowing agent in face and dusting powders and foot powders and baby talc; as a thickening and stabilizing agent in hand lotions, creams, cake make-up, in mineral oil emulsions, in pharmaceutical suspensions, and in depilatories or antiperspirants; as

a thixotropic and thickening agent in ointments and salves, in tooth pastes; as a gelling agent in nasal, surgical and vaginal jellies; and in gelatin capsules to improve extrudability and handling.

Carbopol 940

Carbopol 940, is a fluffy, white powder similar in appearance and over-all properties to Carbopol 934 introduced by B. F. Goodrich Chemical Company, Akron, Ohio. Major difference between the two is the outstanding ability of Carbopol 940 to form extremely clear gels, a possible key to a completely new class of cosmetic products.

The thickening efficiency of Carbopol 940—like that of 934—exceeds that of any other commercially available water-sensitive gum or polymer. Products made with nontoxic Carbopols exhibit excellent body and staying power; Carbopol gels can be easily stirred or pumped during the manufacturing process and can be spread or brushed out easily during use.

The new resin is designed not only to make creams smoother, eliminate drying, caking, and separation of creams and lotions, but also to lend these properties along with unusual gel clarity.

Aluminum Aspirin

Anderson Chemical Company, Division of Stauffer Chemical Company, has completed construction of a new unit at its Weston, Michigan plant for the commercial production of aluminum acetylsalicylate, or, as it is commonly termed, aluminum aspirin. Output of the compound is being sold as the basic ingredient of self-buffering analgesics.

Aluminum acetylsalicylate is a salt which is stable at room temperature. It hydrolyzes in the gastro-intestinal tract to form aspirin and aluminum hydroxide. The aspirin so produced yields typical pharmacological effects; the aluminum hydroxide acts as a buffer and prevents any increase in acidity.

Aluminum aspirin is comparable to aspirin in analgesic, antipyretic and antirheumatic activity. Clinical studies indicate no significant difference in the efficacy of the two compounds. Studies of salicylate excretion and blood salicylate levels indicate that aluminum aspirin is absorbed slightly more slowly than aspirin. However, both are equally completely absorbed and the peak plasma-salicylate level achieved with aluminum aspirin is longer lasting.

An important advantage of aluminum aspirin is its non-acidity. It can be incorporated directly into multi-ingredient tablets because it does not react with many other medicinal agents. Tablets containing aluminum aspirin have no bitter taste so that they can be chewed or used as throat lozenges.

Lipstick Colors Delisted

The 17 D&C red, orange, and yellow certified dyes being considered for delisting (*Drug & Cosmetic Industry* 84:583, May 1959) have, in fact, now been made the subject of an official order transferring these colors to the External D&C category, not approved for lipstick use. The order is dated October 6 and could theoretically be made effective 90 days afterward. According to the announcement "FDA pointed out that the amounts of the colors which may get into the human digestive system when used in lipsticks are much smaller than those used in the animal feeding tests. Under the Federal Food, Drug, and Cosmetic Act, however, the Government must ban the use of any coal-tar color that is harmful in significant amounts in the diet of test animals, even though its use in smaller amounts would be safe.

"The Department of Health, Education, and Welfare has sponsored legislation, now pending in Congress, which would authorize FDA to set limits on the amount of a color which can be safely used, to specify products in which it may be used, or both. Under the present law, if a color cannot qualify as completely 'harmless,' the only way to protect the consumer is to ban it altogether for that particular use."

In fact, the Toilet Goods Association, has requested a hearing, so that actual delisting would not presumably go into effect until after the hearing had taken place, the findings reviewed, and in case of adverse findings, 90 days thereafter. During this period, continued efforts toward the passage of satisfactory legislation can be expected.

Determining Sodium Lauryl Sulfate

At *p*H 3.5 in 3*N* sodium phosphate-phosphoric acid buffer, sodium hypochlorite and *o*-tolidine dihydrochloride react to form a haloquinoid compound, according to H. D. Graham and R. McL. Whitney (*Analyt. Chem.* 31:1673, 1959). When the solution containing this haloquinone is at *p*H 3.0, added sodium lauryl sulfate will couple with it to form a complex giving a purple color with a maximum light absorption at 590 mμ. The intensity of this color is directly proportional to the amount of sodium lauryl sulfate added. High sensitivity and accuracy of determination can be obtained with observance of the established optimal conditions for the test. Of all the variables investigated, the final *p*H of the buffer system seems to be the most critical one for the development of the purple color.

As interfering substances were absent from the particular system for which this test was developed, no specific investigation of other interfering substances was made. However, attention is called to the obvious intereference which would be expected from alkylbenzenesulphonates and other ester sulfates, if present. The presence of oxidizing agents, such as ferric and manganic ions and nitrites, which commonly interfere with the *o*-tolidine test for available chlorine does not interfere unless the combined effect exceeds that of 7.5 p.p.m. of available chlorine. The presence of materials which complex with sodium lauryl sulfate, such as protein, will interfere.

Stabilizing Ascorbic Acid Syrup

Syrups were prepared to contain 15 grams of ascorbic acid in 300 ml. of solution by R. H. Shah and C. L. Huyck (*Drug Standards* 27:110, 1959). One solution contained 120 ml. of 70 per cent sorbitol syrup and 60 ml. of propylene glycol, another 0.75 ml. of a 40 per cent solution of tetrasodium ethylenediamine tetraacetate, and the third contained 0.3 gram of sodium bisulfite. All were made up to volume with U.S.P. syrup. At the end of five weeks, the first solution had shown 1.98 per cent decomposition of ascorbic acid at 10°C., 4.69 per cent at room temperature, and 16.3 per cent at 45°C. Corresponding figures for the second syrup were 5.11, 8.26, and 47.5 per cent and for the third syrup 5.24 per cent, 7.63 per cent, and 44.80 per cent.

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DOW | Chemical news aids beautiful profits

A company calls for reformulation to improve a product's properties . . . or for formulation of new products to round out its line. This happens almost every day; and it can be a king-sized headache for all concerned when ingredient incompatibility rears its ugly head. That's when Dow's Technical Service assistance can quickly help turn a problem into a profit . . . with the right answer and the right chemical at the right time. This article highlights a few such chemicals which are doing beautifully profitable jobs for the drug and cosmetic industry right now.

You may wish to check certain items in this advertisement and forward to those concerned in your company.

ROUTE TO:

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VERSATILE EMULSIFIER EASES FORMULATION, UPS PRODUCT SALABILITY

When formulation of soap-based cosmetic products is the order of the day, Dow triethanolamine is the key to easy, effective emulsification of new and different ingredients. It offers a clear-cut economic advantage, often doing the work which formerly required two or three different agents. It provides a sales advantage for the marketplace, too, because properties of such products as shampoos, aerosol shaving creams and hand lotions can easily be tailored and changed to meet consumer preferences.

Finding the right emulsifying agent is no problem when Dow triethanolamine (TEA) is at hand. So versatile is TEA that this one chemical can replace stocks of many different specialized agents. But it really shines when it comes to improving product properties. In changing formulas, or in developing new ones, wide-range emulsifiers made from TEA provide exact, easy control of emulsion viscosity; at the same time they produce mild emulsions with neutral pH that are easy on the skin.

TEA-soaps produce creams of fine texture and consistency when emulsifying such ingredients as mineral oils, petrolatum, lanolin, vegetable oils and beeswax. Though the effect of the ingredient is retained, the resulting preparation can quickly be removed by washing with water.

The growing trend to modified soap-based formulations for hair shampoos indicates an ideal spot for the use of TEA soaps. For example, TEA oleate is widely used here because it provides excellent cleansing action and high stability of the emulsion. Not incidentally, it greatly simplifies manufacturing operations.

Aerosol shaving creams, too, get a boost from TEA soaps. Low alkalinity means they're noncorrosive to pressurized containers; more important, they won't irritate the skin. These emulsions of oils, lanolin, etc., provide excellent softening, wetting and lubricating action. Shaving creams formulated with a combination of TEA stearate and TEA cocoate have found ready consumer acceptance. And such formulations can be superfatted using an excess of stearic acid.

The emulsion characteristics of TEA-

Triethanolamine soaps speed the manufacture of soap-based products while improving salability and profits.

based hand lotions can be varied to give any desired texture and consistency. And they have the appearance and feel that the customers want—white, unseparating on the shelf, softening and soothing to the skin, readily removed by washing with water.

In the formulation of any soap-based product, a wise first step is the consideration of high quality TEA from Dow. Dow offers valuable Technical Service assistance to pharmaceutical and cosmetic manufacturers in developing special formulations of all kinds. If you have a problem in formulation, consider TEA from Dow. For more information on this versatile chemical, write for a copy of Dow's new booklet "Alkanolamine Soaps in Emulsions".

JACK-OF-ALL-TRADES

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Propylene glycol USP virtually rides off in all directions in its many roles for the drug and cosmetic industry. In pharmaceuticals, it's a first-rate carrier, solvent, emollient, humectant and preservative for such staple items as estrogen and vitamin formulations, antiseptics, salves and ointments. Its solvent ability makes it easy to dissolve prime ingredients and to keep them in solution, even during extended storage. And its preservative action is effective against spoilage organisms, particularly molds and fungi.

These same valuable properties give it a front-row seat in the formulation picture of many cosmetic manufacturers. Often it replaces more expensive ingredients effectively in products such as lotions, creams, make-up, shampoos, suntan preparations, and scores of others.

Dow's new plant at Plaquemine, Louisiana, recently went on stream. This extensive new production facility means there is now plenty of propylene glycol USP available to fill industry's needs.

SPOILAGE FIGHTERS

. . . *save face and profits*

Drug and cosmetic manufacturers rely on Dowicide preservatives to keep shelf goods factory-fresh.

You can count on Dowicide® products to help save your product face . . . and your profits . . . when shelf spoilage threatens. Cosmetics and pharmaceuticals subject to attack by bacteria and fungi can be kept clear, clean and attractive to the shopper when one of these preservative chemicals is in the package! Among Dow's fourteen special Dowicide products there's sure to be one which will solve your preservative problem. For example, Dowicide A or Dowicide 1 are highly effective against spoilage organisms, have a low order of toxicity and irritation.

Whatever the nature of your product, you can depend on Dowicide preservatives to protect it on the shelf . . . help keep its look of purity that helps move it off the shelf by consumer choice.

★ ★ ★ ★

If you're looking for a way to brighten your sales picture, chances are there's a Dow chemical which can help you throw some light on the subject. For more information, write THE DOW CHEMICAL COMPANY, Midland, Michigan, Chemicals Merchandising Department 922AW10.

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Mixed isopropanolamine is an ideal emulsifying agent for cosmetics. It protects against skin irritation and produces creams of good texture, consistency and good color stability.

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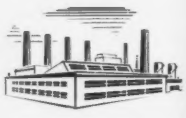
PHYSICIANS	Pleased patients please physicians.	Better taste in orals. Fewer "bitter-taste" complaints from patients.	Smaller dose volume with higher potency solutions.	Less pain with parenterals. Greater patient acceptability.	Fewer complaints from patients. Less wasted time for doctors.	
MANUFACTURING DEPARTMENT 	High and rapid solubility.	Compatible in multivitamin formulae.	Economical, less time and labor in compounding.	No solubilizer needed.	Make clear solutions of 30 mg. or higher per ml. of water.	No special techniques required. Relieve technical department problems.
SALES & ADVERTISING DEPARTMENTS	Better taste; more palatable in high concentrations.	Less pain on injection. Pleased patients ease the doctor's day.	Smaller dose volume required with higher potency solutions.	Pleased physicians are better prospects for other ethical preparations in your line.	*Need a sample and technical data sheet? We'll gladly send both. They're free.*	
MANAGEMENT	New, all-time low price for Riboflavin-5′-Phosphate Sodium Roche .	Economy; lower manufacturing cost raises profit margins.	No solubilizer needed, thus saving extra cost.	Improves present products, makes them easier to sell.	Better your product and you will sell more of it.	Lower inventory costs; less materials required for higher solubility.

TECHNICAL NOTES The theoretical B_2 content of riboflavin-5′-phosphate sodium is 73%. The Roche product has 70 – 73%.

Roche Riboflavin-5′-Phosphate Sodium is identical with the natural flavin mononucleotide which occurs in the "yellow" respiratory tissue enzyme system. Being so, it has immediate biological activity.

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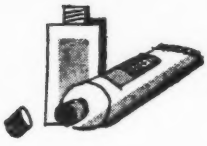

Advancing Therapy

Human Pharmacology.

In the development of new therapeutic agents it is the customary practice to screen the materials in laboratory animals and then proceed directly to a casual clinical trial in patients as a means of deciding the question of introducing a new agent into therapeutics. Neither of these test methods has proved to be sufficiently satisfactory. Materials showing pronounced activity in laboratory animals are frequently ineffectual in human beings. The casual clinical trial is also too often misleading, and an increase in the number of physicians who make it adds little to the validity of the conclusions. It provides only impressions of merit that often fail to materialize, because such trials are made in therapeutic settings in which many factors may operate simultaneously to produce results erroneously ascribed to the new agent itself.

While the controlled clinical trial, with use of scientific pharmacology in human beings, is often used in the more extensive definitive clinical evaluations, it is proposed by T. Greiner et al (*J.A.M.A.* 171: 290, 1959) as a substitute for the casual clinical trial in the earliest screening operations. The virtue of this method of screening is that the results emerge out of an experimental design, that scientific evidence is secured expeditiously and with the use of relatively few patient participants, and that the results are freer of chance and error. A "case history" in human pharmacology is presented to illustrate these views. A group of nine diuretic agents had been proposed for use, some of which aroused enthusiasm and optimism from the results of animal tests and casual clinical trials. In a relatively short period of time, eight of these were eliminated in favor of the most appropriate member of the series for large-scale clinical use.

Screening by the method of human pharmacology is not a common practice. It requires special clinical facilities and personnel especially trained in designing valid pharmacological experiments. Its inclusion in the programs of chemical development with preliminary animal screening for promising therapeutic agents will go far in clearing away the serious obstacle to progress which arises from the premature appearance of new compounds and preparations in the armamentarium of the practicing physician.

New Vasodilator

A new coronary vasodilator has produced marked and definite improvement in 20 of 32 patients with angina pectoris, according to Raymond Harris, reporting in the *American Journal of Cardiology* 4: 274, 1959. The new compound was tested under its laboratory designation of Win 5494 and is still under clinical investigation under Winthrop Laboratories name Myordil. Chemically, it is 3-dimethylamino-1,1,2-tris-(4-methoxyphenyl) - 1 - propene hydrochloride.

Myordil was studied in patients with coronary artery disease who suffered from angina pectoris, myocardial infarction, or some type of arrhythmia. Oral doses eliminated or reduced ventricular premature contractions in 16 of 18 patients; paroxysmal atrial tachycardia was halted in another. No serious side effects were observed in this study.

Declomycin Antibiotic

A new broad spectrum antibiotic with greater antibacterial activity and more prolonged effectiveness than tetracycline has been marketed by Lederle Laboratories Division, American Cyanamid Company.

Trademarked Declomycin demethylchlortetracycline, the new antibiotic has been shown to be gram for gram two to four times as potent as tetracycline. As a result it achieves higher antibiotic activity in the blood with significantly less drug.

Investigators have demonstrated that Declomycin retains antimicrobial activity in the blood 24 to 48 hours longer than tetracycline upon cessation of therapy. In addition, the new drug provides a more sustained and uniform level of antibiotic activity in the blood, eliminating the alternating highs and lows of antibacterial activity seen with other broad spectrum antiibotics. The antibacterial spectrum is similar to that of other tetracyclines.

The new antibiotic is the result of six years of research and development by Lederle scientists. While Declomycin was produced from a mutant strain of the same organism that produced chlortetracycline, it is an entirely new chemical entity.

The daily adult dose is 600 mg. divided into two or four doses. The recommended children's dosage is 3 mg. per pound of body weight daily in divided doses.

Dihydrostreptomycin Toxicity

Shambaugh et al. (*J.A.M.A.* 170: 1657, 1959) have recently reported 32 cases of permanent hearing loss due to dihydrostreptomycin encountered over a period of four years. In many of the cases this has resulted from the use of rather small doses. The most disturbing feature is the list of indications for which the drug was used; most of the patients received it for simple respiratory infections or common surgical operations.

Accordingly, an editorial in the "New England Journal of Medi-

cine" Vol. 261, page 666, 1959) recommends that the use of this antibiotic be discontinued: "There seems to be no good reason at all for continuing to produce dihydrostreptomycin. The Food and Drug Administration and the manufacturers would be well advised to withdraw the agent entirely and to discontinue its manufacture. Little if any value would be lost, and therapeutics would be greatly improved, especially if all packaged combinations of penicillin with either streptomycin or dihydrostreptomycin were abandoned."

Tylosin Antibiotic

Discovery of a new antibiotic reported to have wide potential applications in agriculture was reported to the American Chemical Society meetings by Eli Lilly and Company scientists. The antibiotic is called tylosin.

The new agent, which is relatively nontoxic, is a product of a strain of the actinomycete, *Streptoymces fradiae*. The organisms were isolated from a Thailand soil sample.

Preliminary experiments indicated that low levels of tylosin are highly effective in inhibiting pleuropneumonia-like organisms involved in chronic respiratory diseases of poultry and in sinusitis of turkeys.

Tylosin also has been shown to stimulate weight gains when fed to swine and poultry.

A unique quality of tylosin is that it is converted to a new antimicrobial compound, desmycosin, when allowed to stand in acidic solutions below pH 4. The reaction removes a sugar, mycarose, from the tylosin molecule. Desmycosin is as effective against microorganisms as tylosin and is more stable in acid solutions. Like tylosin, it is relatively nontoxic.

Sodium in Antacids

Since antacids are often prescribed for the relief of gastro-intestinal symptoms to patients on a low-salt diet for other reasons, K. H. Bleifer, J. L. Belsky, and D. J. Bleifer (*N.E.J. Med.* 261: 604, 1959) investigated the sodium content of several commonly used aluminum gel antacids. The four preparations analyzed chemically contained from 4.2 to 5.6 milliequivalents of sodium per 100 ml. of liquid. Intestinal absorption was tested on two subjects maintained on a diet containing approximately 10 milliequivalents of sodium per day and then administered 210 to 300 ml. of aluminum gel antacid daily for three days. Urinary sodium excretion in the subjects increased by even more than the intake from the antacids for an unexplained reason. The authors concluded "unrestricted use of these materials can jeopardize investigative sodium studies as well as therapeutic salt-restricted programs. However, the small concentrations of sodium present are in no way contraindicated in the overwhelming majority of cases in which antacid therapy is needed."

Glutamic Acid Therapy

Striking differences were found by F. T. Zimmerman and B. B. Burgemeister (*Arch. Neurol. Psychiat.* 81: 639, 1959) during comparisons of the relative effectiveness of glutamic acid and reserpine in producing behavioral and psychological test changes in mentally retarded children and adolescents with behavior disorders.

A selected group of 150 subjects with glutamic acid was matched with a corresponding group of 150 subjects given reserpine and 50 subjects given a placebo. Treatment was continued for 6 months.

The average verbal intelligence quotient showed a significant point rise as the result of 6 months of treatment with glutamic acid and only a small rise as the result of reserpine or placebo administration. None of the treatments was successful in raising the performance scores beyond the realm of chance error; results were not significant.

Clinical observations and notes of the neuropsychiatrist before and after treatment revealed that improvement occurred in 126 (64 per cent) of the 196 behavioral traits rated for the group treated with glutamic acid and in 106 (57 per cent) of the 187 traits rated for the reserpine-treated group. When subjects were out of contact and confused at the start of treatment, much better clinical results were obtained with reserpine than with glutamic acid. When subjects were shy, withdrawn, quiet, unresponsive, slow, or depressed initially, glutamic acid was much more effective than reserpine. Reserpine was the drug of choice in patients who were classified as anxious, tense, insecure, irritable, negativistic, or hyperactive, although glutamic acid produced favorable results in a number of instances. Twenty-one (33 per cent) of the 65 traits rated for the placebo-treated group were considered to have improved. However, the much higher ratings obtained by the glutamic acid- and reserpine-treated groups indicate definitely favorable action of each drug, well beyond the limits of personal bias or rating error.

The results support the hypothesis that glutamic acid has an activating action, while reserpine has a more calming or tranquilizing effect. However, individual variabilty of response was extremely wide. From the standpoint of the basic physiochemical mechanism involved, glutamic acid seems to be part of the Krebs cycle, and it would be logical to postulate that the addition of this chemical, as part of this cycle, has a direct effect upon the nervous system.

Phenethylbiguanide (DIB)

Phenethylbiguanide (DBI), a new synthetic, nonsulfonylurea compound, has proved to be an effective hypoglycemic and hypoglycosuric medicament for oral use in the management of diabetes mellitus, according to J. Pomeranze et al (*J.A.M.A.* 171: 252, 1959).

In the study it was found that DBI could be used alone or with a reduced amount of insulin to manage 62 per cent of an unselected group of diabetic patients without regard for the class of diabetes. In 26 per cent of all the patients treated, although good hypoglycemic response was evident, gastrointestinal side-effects necessitated the withdrawal of DBI. However, the incidence of side-effects has been reduced by newer dosing techniques. DBI therapy was discontinued in the remaining 12 per cent of patients in these studies for reasons not related to the effectiveness or side-reactions of the drug.

The sole limitation on the already broad clinical applications of DBI appeared to be its gastrointestinal side-effects. No organ toxicity has been observed in any patient, including those who have been maintained on this therapy for periods ranging through two years.

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Perfumer's Shelf

Kewda Oil

One of the most popular and important perfumes in India is derived from the wild *kewda, Pandanus odoratissimus* L. (fam. Pandanaceae). The long and elliptical flowers, strongly aromatic, usually creamish white or white in color, covered with velvety green and odorous leaves, appear in July and continue flowering till about the end of December every year.

In India, enormous quantities of the flowers are distilled annually for the production of much prized and popular *attars* and aromatic waters, used extensively in perfumes and food flavors, and in the enfleuraged hair oils. Sadgopal first drew the attion of the perfumery world to this important and fascinating new source of essential oil. A special technique was developed for isolation of the volatile oil, yield averaging 0.1 to 0.3 per cent, by extracting the flowers with a solvent, precipitating the fatty and waxy matters with alcohol and distilling off the absolute under reduced pressure.

The oil is a light yellow colored liquid with a very characteristic and fascinating odor reminiscent of lilac super-imposed on hyacinth and tuberose notes. Physicochemical properties of the oil have been reported as follows: $d_{20°}$ 0.9824−1.0880; $n_D20°$ 1.4920−1.5220; $\alpha_D \pm 0°$ to $+2.0°$; acid value (*max.*) 5.0; ester value 16.0−45.0; ester value after acetylation 54.0−142.0; solubility in 90 per cent alcohol, in all proportions.

Chemical composition reported earlier by Sadgopal and later investigated in detail by Deshpande shows that the major constituent of the oil (65 to 80 per cent) is the methyl ether of β-phenylethyl alcohol to which is due the characteristic aroma of the flowers.

The methyl ether prepared by its synthesis from β-phenylethyl alcohol closely resembles the main constituent separated from the natural oil, both in its fragrance and physical properties.

Other constituents are dipentene, *d*-linalool, citral, phenylethyl alcohol and terpene esters.

Some suggestions incorporating the use of *kewda* oil and *attar* in fancy perfumes and compounds are given below:

Base: 15 to 20 per cent solution of either *kewda* oil or *attar kewda* in benzyl benzoate fortified with 20-25 per cent of methyl ether of β-phenylethyl alcohol.

Blenders: Benzyl salicylate, benzyl acetate, art. jasmin, geraniol, phenylethyl alcohol, rhodinol, ylang-ylang oil, linalool, linalyl acetate, gernyl anthranilate.

Modifiers: Dimethyl anthranilate, Wardia, cyclopenta-decanolide, art. tuberose, art. rose, aldehyde C_9 ethyl vanillin, Cyclosia base.

Fixers: Musks (natural and synthetic), *kewda* resinoid, orris absolute 5 per cent.

—Sadgopal, *S.P.C* 32: 80, 1959

Dentifrice Flavor

One of the most important ingredients in toothpaste is flavor. It is, from a commercial point of view, one of the factors on which most of the advertising used today is based, and one which will continue to rank high in the process of selection by the consumer.

In the early days of dentifrice manufacture, peppermint oil or spearmint oil were the flavoring agents used almost exclusively. Some menthol was added to enhance the desired freshening effect.

Toothpaste manufacturers have, in recent years, practiced greater discretion in the selection and application of flavors for their products. The basic ingredients of modern dentifrices are known to possess a rather unpleasant taste. This fact has, therefore, created new problems for the flavor chemist, who no longer has recourse to the conventional type of toothpaste flavors. The characteristic peppermint or spearmint flavors, even in their most refined quality, can no longer serve the function of general flavoring. The best flavor compound, in most cases, cannot give the quality or character desired if one or more of the toothpaste ingredients are incompatible with the flavor material.

In his initial study, the flavor chemist evaluates the general organoleptic impression of the unflavored toothpaste base. Using his knowledge of and experience with the essential oils, isolates, derivatives and, above all, the flavomatics at his disposal, he creates the flavor compound that will successfully render the dentifrice palatable and refreshing.

Mint, spice and herb type essential oils form the bulk of the materials used in flavor formulations. The judicious addition of aromatic chemicals, even in trace amounts, can enhance the rendition of these flavors, giving them harmony and balance. Experience has taught the flavor chemist that, in the absence of the proper flavomatics, those essential oils which characterize the flavor in a given dentifrice, would lack appeal, would show evidence of being unbalanced, and would often appear harsh.

Very interesting flavor specialties are available, either as basic flavomatics or as compounds, that will serve to "condition" or "fix" a given dentifrice flavor. There is no preestablished guide or rule of thumb than can assure the successful performance of a flavor in a given toothpaste without first trying it. It is absolutely necessary that the flavored product be subjected to tests of sta-

bility, discoloration, viscosity, moisture-loss, and others for a proper period of time before the flavor can be termed fully compatible with and suitable for the paste involved.
—*Givaudan Flavorist*

Wine Lees Oil

Wine lees oil is one of the few products which has the bouquet and odor of wine. The preparation and properties of wine lees oil have been described and the details of the composition of the oil are reported by Dehaux and Belian (*Riechst. and Arom.* 9: 97, 1959). The free fatty acids have been identified as being composed mainly of pelargonic and decylic acids which also occur in the oil in the form of their ethyl esters. Another ester found is probably ethyl caprylate. The aldehyde content of the oil was found to be 0.42 per cent calculated as decylic aldehyde.

Linalol and Linalyl Acetate

Linalol and its acetate ester is described by H. K. Thomas (*Dragoco Reports* 6: 162, 1959). The alcohol is an unsaturated terpene alcohol with the empirical formula $C_{10}H_{18}O$. Although it exists in the *alpha* and *beta* isomeric forms, these have not yet been isolated in pure form because they readily isomerize to other terpene alcohols. Linalol is present in many essential oils, as either the dextro- or the levo-rotatory form. It is present, for instance, in linaloe or bois-de-rose oils from Mexico, Cayenne and Brazil, ho or shiu oil, coriander, lavender oils, lavandin, bergamot, petitgrain oils, muscatel sage oil, spike lavender, nutmeg, geranium, hop oils, Ceylon cinnamon, lemon, and sweet orange oils, etc. It is especially important in a number of important flower oils, including orange flower (neroli), rose, ylang-ylang, jasmin flower, champaca flower, gardenia, jonquil, and cassia flower oils.

The pure oil is transparent and colorless, with a delicate, sweet odor resembling that of lily-of-the-valley. It is completely stable in soap and is not discolored by alkali. Its fine odor is at best advantage in the purest oils, free from by-odors, which are the result of newer production methods. The alcohol is utilized extensively in formulating soap perfumes and in the florals such as lily-of-the-valley, sweet pea, lilac, jasmin, orange flowers, and in some flavors.

Linalyl acetate is also present in many essential oils and is a major component of bergamot and lavender oils. Only modern production methods have made the 100 per cent pure material available, while the 80 and 90 per cent modern products are superior to older esters in being free from other esters and terpenes; The result is products with a much finer and cleaner odor. Linalyl acetate is a transparent and colorless liquid with a fruity odor resembling that of bergamot oil.

Bergamot Oil

The composition of bergamot oil is more complex than has been hither-to been believed, according to F. LaFace (*Parf. Cosm. Savons* 2: 341, 1959). Althought the olfactory note is dominated by linalyl acetate and linalol, which constitute 60 to 70 per cent of the oil, and the intensity of the odor is in direct proportion to the linalyl acetate content, other substances are often present which, even in small quantities, contribute to the bouquet and may even bring about variations caused by degree of maturity, geographic source or extraction techniques. Moreover, it is well known that bergamot oils from certain localities, in spite of their lower ester content, are particularly in demand because of their fine bouquet.

Using modern methods of investigation, we found that along with linalyl acetate, the only ester whose presence has been certainly demonstrated, there are three other esters, although in small quantity. New alcohols have not yet been identified, but the carbonyl compounds include citral, whose presence was considered probable, and also three higher fatty aldehydes.

Since the proportion of oxygenated products accompanying the major constituents, linalol and its acetate, is very small, while the effect on the odor may be quite noticeable, these may be compounds capable of modifying and improving the bouquet of an oil which cannot be reproduced by simply mixing the constituents identified by usual analytical methods. The importance of these trace components can be deduced from the fact that oils obtained from very ripe fruits, although very rich in linalyl acetate, have a less aromatic and flatter odor. Investigation has further shown that minor oxygenated constituents are present in all samples examined, but in variable amounts.

It is also possible that "negative olfactory substances" may be introduced into the oil by the condition of the fruits or by bad processing. Unripe fruits, for instance, give an oil with a sharp odor and a green note, and bad consequences follow excessive grinding. Chromatographic studies have shown that the nonvolatile bergamot oil residue contains, along with coumarin compounds, a substance with a sharp and disagreeable odor.

Perfume Design

Perfumes may generally be designed along two lines, according to E. Gorokhoff (*Parf. Cosm. Savons* 1: 138, 1958). First, if synthetics are used to a considerable extent, the evaporation curve will be very straight; second, with large proportions of natural oils, the evaporation line will be curved, the extent depending upon whether a light or heavy oil is used. Generally, more synthetics than natural oils are used to obtain a relatively straight line evaporation rate, but still maintaining roundness of odor. It is certain that the ideal perfume is one hich retains its character from the beginning to the end of its evaporation, but this is most difficult to obtain. A good perfume must maintain an equilibrium between natural and synthetic bases, since synthetics confer originality, natural oils give richness and distinction to the blend.

Corphos (Crookes-Barnes) is a 0.5 per cent ophthalmic solution of hydrocortisone-21-phosphate, available in 2.5 cc. dropper bottles.

Neo-Polycin Otic (Pitman-Moore) is an ear drop preparation supplied in 8 gram bottles. Each gram contains one per cent of dyclonine hydrochloride, 2 mg. of neomycin as the sulfate and 4000 units of polymixin B sulfate, combining two antibiotics with a topical anesthetic.

Endrate Disodium (Abbott), 3 grams in 20 cc. ampoules, is dissolved in isotonic saline or dextrose for intravenous infusion in the treatment of pathologic calcification.

Erythrocin Ethyl Succinate Oral Suspension (Abbott) is citrus flavored, each 5 cc. teaspoonful providing 200 mg. of Erythrocin. Supplied in 60 cc. bottles.

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Skin Research

Sebum Fatty Acids

A study of the composition of the fatty acids from samples of the skin surface lipids from different individuals and from different areas of skin and at different times from the same subject by B. Boughton and V. R. Wheatley (*J. Invest. Dermatol.* 33:49, 1959) has shown a general constancy in composition. Some differences, however, have been observed.

There appeared to be a slight difference between men and women but this seems to be due more to greater individual differences among the women rather than to a definite sex difference in sebum composition. Children generally have less unsaturated C_{16} acid and more of all three types of C_{18} acids than do adults.

The fatty acid composition of the skin surface lipids from the same area of skin of the same subject showed little variation over periods up to 5 months. No change in composition appears to occur during the menstrual cycle in women. Lower values were observed for the unsaturated acids in the surface lipids from the extremities as compared with those from other skin areas of the same individual. It was observed that the percentage of unsaturated acids also fell as the sebum level dropped. The lower results for the arms and legs are therefore probably due to the lower sebaceous activity in these regions rather than to definite differences in the composition of the sebum secreted by the different areas of skin. The skin surface lipids arise from two different sources, the keratinizing cells of the epidermis and the sebaceous glands. With most adult individuals the contribution by the epidermal lipids to the surface lipids from areas of skin on the trunk is negligible. However, in the surface lipids from the extremities of adults and from all areas of skin from children and certain adults with 'dry' skins the contribution by the epidermal lipids becomes appreciable due to the much lower sebaceous activity of these skin areas. By relating the sebum level with the content of the various groups of fatty acids in the surface lipids it has been deduced that the saturated acids originate mainly from the epidermis, the unsaturated acids from the sebaceous glands and the highly branched acids from both sources. Recent analyses of the fatty acids of epidermal lipids has confirmed that these lipids contain less unsaturated acids than do the surface lipids but the presence of significant amounts of highly branched acids could not be demonstrated.

Lower results for the unsaturated acids were obtained when the swab method was used for collecting the samples of surface lipids as compared with the cup method. For fatty acid studies of the surface lipids the latter method of collection should be used, and, to avoid appreciable dilution with epidermal lipids, the site chosen for collecting the sample should be the back.

Analysis of the composition of the skin surface lipid fatty acids from subjects with acne vulgaris, both before and after treatment by B. Boughton et al (*J. Invest. Dermatol.* 33:57, 1959) failed to reveal any abnormality in sebum composition in this disease. In one of four cases of seborrheic dermatitis, however, the proportion of unsaturated acids in the sebum was significantly lower than the values for normal subjects, with a return to more normal values after treatment.

Analysis of dietary fats and feeding experiments of chocolate to hairless rats has failed to show that the deleterious action of chocolate and pork fat in acne vulgaris is due to alteration of the sebum composition by these fats.

Skin Cornification

The cornification of the epidermal cells is the process which forms the relatively inert, protective, outer barrier of the body surface. It is a process in which the epidermal cells, passing from the basal layers to the surface, first change their shape and then quite suddenly lose their cellular organization and become the flattened uniformly filled cells of the horny layers. The chemistry and histochemistry of cornification has been much studied, and one cannot but marvel how the originally heterogeneous cell contents come to form such an apparently uniform end-product.

Laden *et al.* have described electron microscopic observations of the kerato-hyalin granules, and have related them to keratin formation.

A description is given by A. Charles (*J. Invest. Dermatol.* 33:65, 1959) of the changing appearance of cells in the cornifying layers of the epidermis of human skin observed in the electron microscope. Beginning with the appearance of kerato-hyalin, the continuous precipitation of insoluble material is followed until the fully cornified squame is formed. Two separate processes seem to occur, of which one is probably keratinization in the sense used by Astbury and Dickinson; the other seems to result in non-fibrillar material.

Topical Decadron

Six new high-potency topical steroid products, four of them specifically designed for ophthalmic use, have been released by Merck Sharp & Dohme, Division of Merck & Co., Inc. Each of the products contains 'Decadron' Phosphate (dexamethasone 21-phosphate).

The new line of products consists of an ophthalmic ointment, an ophthalmic solution, and a topical cream of the steroid alone, and the same package sizes and dosage forms containing the steroid and neomycin sulfate in combination.

(*Continued from page 457*)

such as penetration of sulfonamides into an agar gel; histological examination, as in the determination of keratolysis following penetration of salicylic acid; tracer techniques utilizing dyes, fluorescent and radioactive compounds; observation of physiological changes such as wheal formation, relief of pruritis, production of anesthesia or alteration in the activity of the sweat gland; specific quantitative methods including chemical analysis of the skin, urine, blood, or an internal organ, determination of the loss of a substance from the cutaneous surface. Very few methods used have given a true measurement of the number of molecules which penetrate a unit area of the skin in unit time. The methods seldom reveal the localization of a substance which does penetrate.

Diffusion of a substance through the skin, unlike that through a thin membrane, does not rapidly reach a steady state, and continuous measurements are therefore necessary in a complete study of percutaneous absorption, according to *M. Ainsworth* of the Ministry of Supply, London. Such measurements on the intact animal must relate to the accumulation of the penetrating substance in the body or to its rate of disappearance from the skin surface. In either case, the quantities involved are usually so small that highly sensitive methods, such as those using radioactive tracers, are necessary.

Because of its low metabolic activity, however, the skin can be isolated for use in direct studies of permeability. In addition, the amount of penetrating substance entering the skin blood vessels can be measured when the vascular system of the isolated skin is perfused with physiological fluid. Such a preparation has been used to study the effect of blood circulation on the rate of percutaneous absorption. Surface clearance is considered to be a convenient and reliable means of studying absorption into human skin.

Autoradiography has proved to be a valuable tool for determining the presence of radioisotopes in histologically prepared skin sections. A new method was presented by *Dr. B. R. Choman* of Lever Brothers to demonstrate the location of small quantities of radioactive substances in the skin resulting from topical application.

Data showed that sodium lauryl sulfate is absorbed readily into the dermis of living skin. Application of the tagged detergent to dead or excised skin results in very superficial absorption involving the stratum corneum only.

Protection, the chief function of the integument, is largely dependent upon special structural features of the epidermis. The toughness of the fibrous protein, keratin, in the external horny layer of the skin withstands direct shearing and friction. At the base of the horny layer is a barrier 10 microns thick which prevents penetration of molecules of larger than 200-300 molecular weight. The significant features of this main barrier according to *Dr. R. D. Griesemer* of the Harvard Medical School, are the tightly packed arrangement of its cells and the closely knit keratin mesh within these cells. Penetration of small molecules through the barrier is further restricted by the interaction between charges on the penetrating molecule and the barrier layer molecules. The few molecules which do penetrate are either bound by the living epidermis or dermis or carried away by tissue fluids to the lymphatic and blood vessels. Thus, for a substance to exert a biological effect on intact skin, it must do so in a very low concentration.

If the structure of the barrier is modified physically or chemically, penetration increases. Very large increases occur after simple scratches, burns, vigorous stretching, exposure to alkali or lipid solvents, or in inflamed skin. Repair of the barrier occurs within 24 to 48 hours by the sudden alteration of the dying epidermal cells beneath the barrier.

Various factors governing the rate of skin penetration by chemical agents were considered from the physical chemical viewpoints by *Dr. T. Higuchi* of the University of Wisconsin. Although the exact mechanism responsible for percutaneous absorption through intact skin is still open to debate, many useful relationships can be deduced on thermodynamic bases which are valid irrespective of the nature of the transfer process leading to absorption. The influence of *p*H, solvent power, temperature and viscosity of ointment bases and the effects of concentration, solubility, thermodynamic properties, diffusivity, etc., of the active medicament in determining the rate of absorption were considered.

The effectiveness of hormone cosmetics can be gauged according to *Dr. Max A. Goldzieber* by serial biopsies or by spectrophotometry of reflected light. The increased resilience or elasticity of the skin after application of hormones has also been measured.

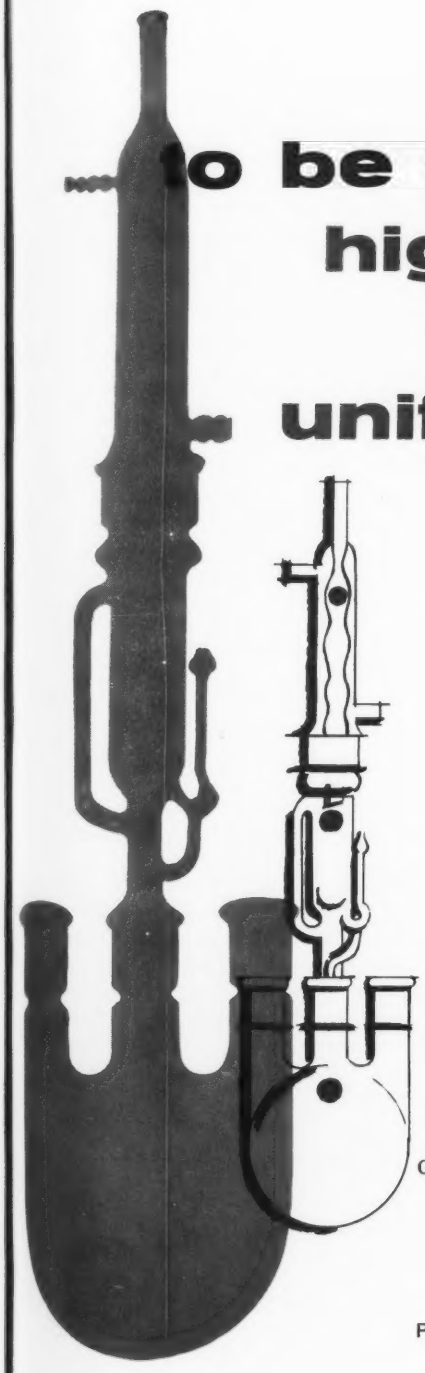
Estrogens have given demonstrable results in the treatment of the aging changes of the female skin and in the treatment of acne in both sexes. The topical application of estrogen in acne is adequate only in the milder cases.

The percutaneous absorption of hydrocortisone was first conclusively demonstrated by the detection of urinary radio-activity following application of C^{14}-labeled hydrocortisone to normal skin.

Cortisone, which is therapeutically ineffectual when topically applied, penetrates normal skin in amounts approximately equivalent to hydrocortisone. The disparity in therapeutic effectiveness between these hormones suggests the possibility of different metabolic pathways for each compound in the skin. Initial studies confirming this and implications of these findings were discussed by *Dr. Frederick D. Malkinson*, of the University of Chicago.

Various salicylates were applied to the clipped ventral surfaces of anesthetized rabbits and plasma levels

(*Continued on page 574*)



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The Actinomycetes, Vol I—Nature, Occurrence, and Activities, *by Selman A. Waksman, 327 pp., Illus., The Wiliams & Wilkins Co., Baltimore, (1959), cloth,* **$12.50.**

No other group of microbes, and for that matter no other group of living systems, whether of plant, animal, or microbial origin, has been in recent years the focus of so much attention by the investigator, especially the microbiologist, the chemist, and the medical scientist, and by the pharmaceutical manufacturer, as the actinomycetes. This increased attention is due primarily to the discovery that the actinomycetes comprise many forms that have the capacity to produce a large number of chemical substances capable of inhibiting the growth of microorganisms, especially disease-producing forms. The rapid accumulation of basic knowledge concerning the actinomycetes well justifies this comprehensive treatise at this time.

The Effect Of Pharmacologic Agents On The Nervous System, *488 pp., Illus., The Williams & Wilkins Co., Baltimore, (1959), cloth,* **$13.50.**

The Association for Research in Nervous and Mental Diseases offers this compendium of its 1957 Proceedings on "The Effect of Pharmacologic Agents on the Nervous System." Contained in it are the clinical experience, considered evaluations, and aspects of the research activity of many outstanding investigators, as well as reviews of the literature. The range of topics included and their bearing one upon another attest to the closer reapproachment of psychiatry, neurology, and medicine and the disciplines which nurture them. The discussions themselves, though they reveal at times wide differences of opinion as to method and interpretation, also reveal substantial areas of agreement. They certainly convey the general feeling that pharmacologic agents are here to stay, not only because of their clinical value, but also because of their potential value in illuminating the somatic substrate of human behavior.

The Sequestration Of Metals (Theoretical Considerations and Practical Applications), *by Robert L. Smith, Ph.D., 256 pp., The MacMillan Co., New York, (1959), cloth,* **$8.50.**

After defining sequestration and explaining the nature of dative valency, the author considers the chelate ring and the influence of ligand and metal on strength of bond. General consideration of competitions in chelate systems is followed by the chemical and physical properties of the various types of sequestering agents. Applications of these materials are considered, first, from general principles and, afterwards, under specific industries, analytical chemistry, and the biological sciences. Industrial applications include agriculture, chemical industry, cosmetic and pharmaceutical applications, foodstuffs and beverages, and the like.

The Nursing And Management Of Skin Diseases, *by D. S. Wilkinson, M. D., 288 pp., The MacMillan Co., New York, 1958, cloth,* **$5.75.**

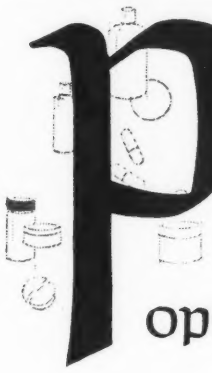
This handbook describes in detail the many practical procedures needed by the doctor and the nurse in their everyday management of the patient with a skin disease. The book contains sections on the general principles of the behavior of the skin, the management of a number of common diseases, particular problems that arise in the nursing of skin patients, and special techniques used in diagnosis and treatment. There is also a most useful formulary.

Phenolic Resins, by David F. Gould, The Borden Chemical Co., *213 pp., pocket size, Reinhold Publishing Corp., New York, (1959), cloth,* **$5.75.**

This is a presentation of the raw materials, production methods, and applications of the phenolic resins. The book emphasizes the practical features, including commercial and economic considerations. It describes each major field of application in separate chapters, and is up-to-date in every respect.

The Human Integument, *edited by Stephen Rothman, 260 pages, American Association for the Advancement of Science, Washington, D. C., Cloth,* **$5.75.**

This is the bound volume of papers and discussions presented at the symposium at Indianapolis, December 1957, in connection with the meeting of the American Association for the Advancement of Science, and co-sponsored by the Committee on Cosmetics of the American Medical Association and the Society for Investigative Dermatology. The presentation is divided into sections, first, The Integument as an Organ of Protection, which includes the papers "Relation of the anatomy of normal and abnormal skin to its protective function," by Richard B. Stoughton; "Protection against the transfer of matter through the skin," by Robert D. Griesemer; and "Protection against the invasion of bacteria and fungi," by Irvin H. Blank. The next section, Circulation and Vascular Reaction, includes "Structural aspects and hemodynamics of microcirculation in the skin," by Benjamin W. Zweifach; "Physiology of cutaneous circulation, thermoregulatory functions," by Alan C. Burton; "Pathology and therapy of cutaneous circulatory disorders," by Robert R. Kierland. The third section is devoted to Sebaceous Gland Secretion, with papers on "Significance of changes in pilosebaceous units in acne and other diseases," by Eugene J. Van Scott; "Biochemical and hormonal aspects of sebaceous secretion," by Allan L. Lorincz; "Pathogenetic, therapeutic, and cosmetic considerations in acne vulgaris," by Marion B. Sulzberger. The final group of papers covers Pathogenetic Factors in Premalignant Conditions and Malignancies of the Skin, with papers on "Etiologic factors and the pathogenesis of premalignant and malignant lesions of the skin," by Raymond B. Suskind and A. Wesley Horton; "Clinical, histologic, and differential considerations," by Hermann, Pincus; and "Prognosis, preventive measures, and treatment of premalignant conditions and malignancies of the skin," by Frederick D. Malkinson. This book is vital to all interested in the fundamentals of skin and cosmetics.



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Trade Literature

Hexachlorophene Bibliography

Sindar Corporation, 321 West 44th St., New York 36, N. Y., has published a supplement to its Technical Bulletin H-1, entitled G-11 (Hexachlorophene U.S.P.)—A Supplementary Bibliography. The annotated bibliography appears in Sindar Reporter Number 3, 1959, and includes abstracts of 23 articles and four patents. An index is included.

From Chemicals to Coatings

The 1959-1960 edition of The Dow Chemical Company's general catalog is now available from Midland, Mich., or any Dow sales office. The 44-page compilation, Products of The Dow Chemical Company, lists the properties and uses of some 375 industrial, pharmaceutical, and agricultural chemicals currently produced. It also has an expanded section on plastics and coating products, as well as sections on such products as textile fibers and automotive chemicals.

Filling Equipment

Popper & Sons, Inc., 300 Fourth Ave., New York 10, N. Y., have published Bulletin #659F, describing their newly expanded line of cosmetic and pharmaceutical filling equipment. The new units, some of which have already been installed in plants, are "custom built" for the user's requirements.

Metal Containers

The J. L. Clark Manufacturing Company, 2300 Sixth Street, Rockford, Ill., has made available a booklet, Traveling through Clark with Containers Designed to Sell on Sight, which describes through pictures and captions the entire process of producing containers—from the initial conference with a customer through layout, tooling, lithography, and fabrication of the containers themselves. The special techniques used for producing high-quality lithography on metal while keeping costs down are described.

Olefin Polymers

A new brochure, Marlex, Its Growth—Your Opportunity, illustrating applications and characteristics of the Phillips family of olefin polymers, has been issued by the Phillips Chemical Company, Plastic Sales Division, Bartlesville, Oklahoma. The 26-page report in color describes the more than 400 Marlex items now in existence, and suggests new applications.

Auto Fleet Leasing

A study, Advantages and Disadvantages of Auto Fleet Leasing, has been published by the Foundation for Management Research, 121 West Adams St., Chicago 3, Ill. It is based on company records covering 29,264 cars of which 8,926 were salesmen-owned, 8,347 were company-owned, 11,901 were leased to auto fleets.

Laboratory Equipment

The Modern Laboratory Equipment Company, Inc., 1809-11 First Ave., New York 28, N. Y., has published a new catalog covering its drug and pharmaceutical laboratory equipment.

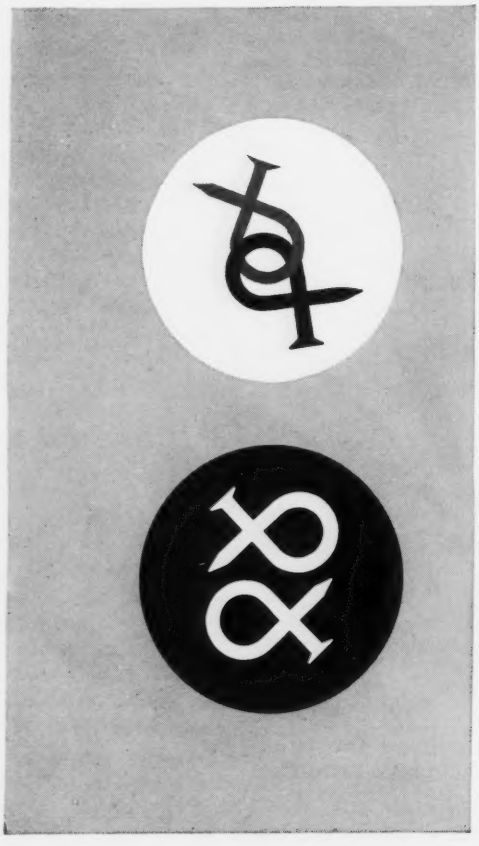

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TABLE 2
Materials for Punches, Punch Tips, Punch Inserts, Punch Holders and Core Rods

No.	Hardness Rockwell C	Characteristics: Wear	Characteristics: Toughness	Cost index	Recommended for
3	54-56	Fair	Excellent	100	Single and rotary punches—bevel edges—std. shallow and deep concave. Special shape punches, punch holders and threaded parts.
3X	Tip 48 Body 52-54	Fair	Excellent	100	For extra deep, concave punches, modified ball shapes, thin edges.
4	56-58	Good	Good	120	Single punches—for heavy pressure applications. Not recommended for sharp edge punches, deep concavities, etc.
5	60-62	Good	Fair	120	For core rods ½" diameter or larger.
5B	60-62	Good	Good	120	For core rods up to ½" diameter.
6	Punches 57-59, Core rods 62-64	Very good to excellent	Poor	150	Long run and abrasive applications. For insert punches and core rod tip. No's 15 or 54 preferred for solid punches but satisfactory for large diameters and plain faces. Life 6 to 10 times that of No. 3.
15	55-57	Very good to excellent	Fair to poor	150	Same as for No. 6. Has 90% of wear resistance of No. 6 but not as brittle.
23	56-58	Good	Good to very good	120	Similar to No. 4 but slightly tougher.
29	55-57	Good	Poor	130	Corrosive applications—punch inserts, solid punches. Punch holders—not recommended for deep concavities.
54	57-58	Very good	Fair	130	Abrasive applications and long runs—single and rotary punches std. concavities. Life 2 to 3 times that of No. 3; tougher than No. 6 and No. 15; more brittle than No. 4.
Stellite	45-55	Very good to excellent	Poor	400	Corrosive applications. Punch tip and punch inserts.
Tungsten Carbide	80-85	Excellent	Very poor	300	High abrasive and long run applications. Not recommended for corrosive applications. Used for punch tips, punch inserts and core rod tips (10 times or more the life of No. 6).
2	61-63	Fair	Poor	100	Small single and rotary dies. Not recommended for special shapes, shoulder dies, large dies or high pressures. Case about ⅛" deep—bends under high pressure.
3	49-52	Fair	Excellent	100	Insert die cases and threaded parts.
5	50-62	Good	Poor to fair	120	Single and rotary dies. For intricate shapes, squares, triangles, etc. Wearing qualities about 20% better than No. 2.
6	62-64	Very good to excellent	Poor to fair	130	Single and rotary dies. For long run and abrasive applications (6 to 10 times the life of No. 2 and No. 3).
15	59-61	Very good to excellent	Fair	130	Single and rotary dies. For intricate shapes, squares, triangles, etc. Minimum shape distortion when heat treated. Similar to No. 6, 90% of wear resistance but not so brittle.
29	59-61	Good	Poor	135	For corrosive applications. Rotary and single punch dies.
54	60-61	Very good	Good	130	Single and rotary dies. For abrasive applications and long runs. Does not change shape in heat treating. Tougher than No. 2.
Stellite	45-55	Very good to excellent	Poor	400	For corrosive applications. Rotary and single punch dies.
Tungsten Carbide	80-85	Excellent	Very poor	300	For highly abrasive and long run applications. Not recommended for corrosive applications. For die inserts (10 times or more the life of No. 6).

(*Continued from page 470*)

through the use of holders and inserts. Holders and inserts are initially more expensive than solid punches, but if punches are subject to excessive wear or to frequent breakage, the holder and insert combination may be more economical because replacements are usually limited to less expensive inserts. The use of holders and inserts is usually confined to punches with small diameters or for compacting very abrasive materials.

Finishes

Ordinarily, requirements for finish on the face, head, and shank of the punch are seldom considered when comparing punch and die quotations from alternate sources. But finish is a more important factor than is usually realized. Inferior finishes may eventually result in more frequent replacement of punches and dies as well as of cams and pressure rolls due to galling, may require more frequent cleaning due to material "pick-up," and may produce tablets of inferior appearance.

It has been our experience that a nominal amount of additional investment in finish is sound. We recommend, and normally provide, finishes of 12 microinches on punch heads, 5 microinches on punch shanks, and 2 microinches or better on punch faces.

Tools are occasionally supplied with what is commonly called "satin" finish. One method of obtain-

(*Continued on page 544*)

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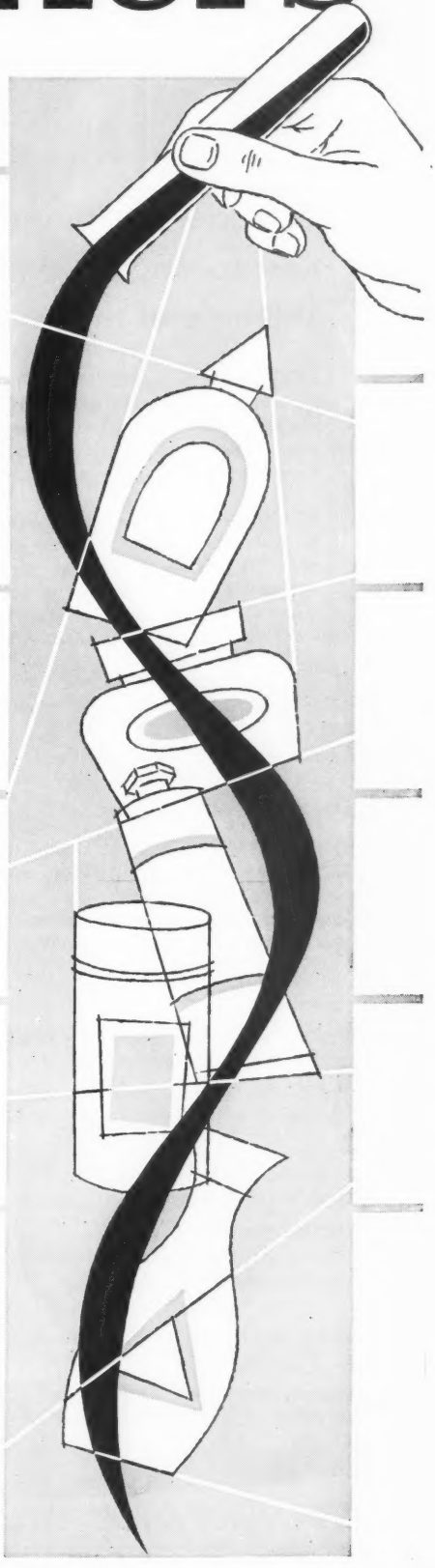

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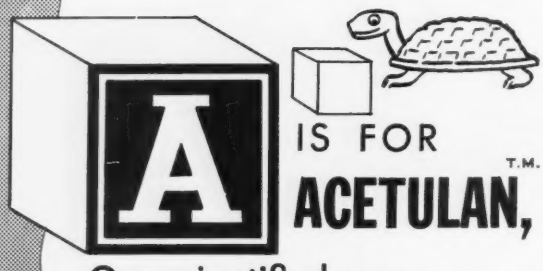

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AMERCHOL PARK — EDISON, N. J.

(*Continued from page 542*)

ing a satin finish is through liquid honing, which gives a smooth, grayish appearance to the metal, resembling that of a worn punch face. Such a finish shows up on the profilometer as a pebbled surface. When two satin surface finishes rub together, point-to-point contact results, rather than surface-to-surface contact. There are a limited number of applications where satin finish is actually beneficial, but it must be selected with judgment.

Comparative merits of different finishes are difficult to evaluate in terms of actual performance because of the large quantity of tablets that can be produced over a long period of time even with tools having inferior finishes.

Clearances and Fits

Clearances and fits between punches and dies are also significant factors. There is no single standard clearance that meets all conditions. The ideal design provides as close a fit as possible to allow for maximum wear. However, certain materials under certain pressure conditions require greater initial clearance in order to prevent binding. Also, clearances must sometimes be modified in order to obtain maximum utilization of some of the high-speed tabletting machines now on the market.

Clearances and fits are also highly important from the standpoint of tool interchangeability. This applies particularly to the tooling for special shapes. When buying special shape punches and dies for rotary tablet machines the buyer should carefully examine the claims made by tool suppliers that they can guarantee complete interchangeability, which means that *any* punch can be used with *any* die. This specification can easily be met by simply allowing sufficient clearance between all the punches and dies. However, many tools sold under such claims have so *much* initial clearance that even before they are set up in the machine their potential life has been substantially reduced. A difference of even as little as 0.0005 inches in clearance can mean a difference of millions of tablets in total production.

Interchangeability may not actually be required. We have found that after a set of special-shape tools for a rotary press has been used in production, each punch and die station takes on certain slightly different characteristics due to slight variations in the machine itself. When such tools are removed from the machine and re-run at a later date, better results are obtained if each punch and die is re-installed in the same punch and die socket in which it was run originally. This would appear largely to nullify the theoretical value of complete interchangeability of all tools. Therefore, Stokes normally manufactures special-shape rotary tools in matched marked stations rather than matched sets. This permits closer tolerances and results in longer tool life. However, com-

(*Continued on page 546*)

Reader's Questions . . .

Skin Coloring: *I have seen local promotions for a preparation which when regularly applied to the skin is supposed to darken the skin color gradually until the effect of a light or heavy sun tan is reached. This is a simulated tan, apparently not affecting the actual skin coloring and not resulting from sunburn nor followed by skin peeling. Can you give me any suggestions as to the active ingredients in a preparation of this kind?* ATLANTA

I have seen publicity material about the preparation you describe, but know nothing further about it. Assuming the claims are borne out, a number of approaches are possible. First there is the use of a certified dye mixture to stain the skin, but there is certainly nothing very special about this method. Next, it might be possible to apply to the skin specific stimulants or precursors for natural pigment formation. Psoralen derivatives, for instance, work in this manner, but this type of action, altering the skin, would be a drug action under the law and would require label information concerning the active ingredient. Finally, a clear and colorless solution might contain compounds which darken when affected by the air or by skin enzymes. Whether or not compounds of this nature could get past the color provisions of the Food, Drug, and Cosmetic Act is a matter for serious consideration. A few possibilities, not necessarily the right ones, come to mind. For instance, anyone doing photographic work is aware of the straining potential of photographic developers other than paraphenylene diamine. These have certainly been fully exploited in hair dye formulation and would not represent a new preparation. Salicylaldehyde, although itself colorless, will leave a powerful bright yellow stain on the skin; ancient inks consisted of mixtures of ferrous salts and gallic acid, but the oxidation product is blue-black. Leuco dyes, oxidizing on the skin, might be used. In all instances, the problems of dye certification and skin irritation will require the most careful investigation.

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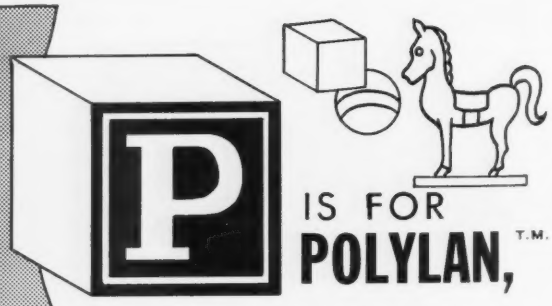

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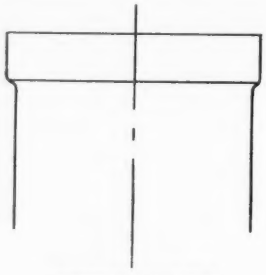
(*Continued from page 544*)

plete interchangeability of tools can readily be provided, if required.

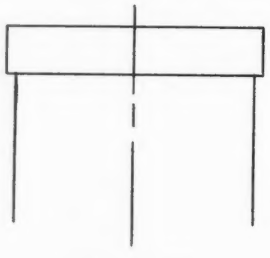
Scrape-Off or Relief

Certain types of material tend to accumulate or build up between the lower punch tip and the die wall. This leads to binding of the lower punch in the die, causing hard pull-down and hard ejection. This in turn results in wear of the cams and pressure rolls and produces galling or pitting of the punch heads. To ameliorate this condition, various types of scrape-offs or reliefs are available with lower punches. As with finish and clearance, the proper type of relief can make the difference between an efficient tabletting operation and an inefficient one.

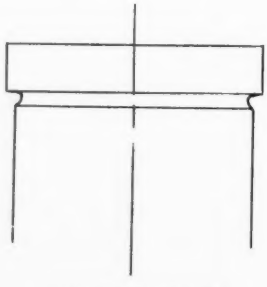
Many materials present no problem of the punches binding in the dies, and standard relief is all that is required. This consists of a slightly rounded and polished edge at the point where the punch shank tapers down to conform to the punch tip diameter.



STANDARD RELIEF



SHARP RELIEF



BAKELITE RELIEF

Some materials, on the other hand, operate better with a sharp relief. This consists of a knife edge that tends to cut the material free as it builds up on the die walls. Still another type of relief is referred to as

"Bakelite" relief because it was originally developed for Bakelite pre-forms. This not only embodies a knife edge but also an undercut and taper for the purpose of keeping the die walls clean. These three represent the most commonly used types of relief. However, there are a number of others of a special nature that have been successfully used on other problem applications. Here, again, the buyer can profitably draw on the knowledge of the equipment manufacturer to design and provide tools that require a minimum of cleaning during production runs.

Sources of Supply

In buying tools for rotary- and single-punch tablet machines, all buyers will naturally take price and delivery into consideration. If price and delivery are the *sole* purchasing criteria, however, small machine shops may sometimes be placed in what appears to be a slightly favorable competitive position. Such shops, although they have never seen a tablet machine in operation, may not only be willing to shave prices in order to pick up an account, but may be able to supply certain tools completely in accordance with specifications. However, once a company has started down the path of dealing exclusively with small machine shops, it may be trapped by any one of a number of pitfalls that eventually results in a less efficient tabletting department.

By such dealings, for example, the customer may well lose contact with the constant stream of technical progress in tabletting procedures, and thus miss the benefits such knowledge could bring to the refinement of his operations.

Moreover, he will not partake of the free exchange of information between different industries or different firms in the same industry—which an industry itself often does not provide but for which the specialist in tabletting does provide a medium—by which the problems of one industry are often solved by solutions developed years before in another industry.

Very few users of punches and dies have statistical data available that tell them the comparative number of tablets that can be produced from similar tools obtained from different sources of supply. This is an extremely important consideration and should be given more attention. The number of tablets produced can easily vary more than 100 per cent using *what appears to be* the same type of tooling from different sources.

As must be clear from the foregoing review, production tools for tablet machines are specialty products. They require a different set of buying standards than items such as electrical switches, gaskets, and oil seals. There are other very important considerations involved in purchasing this kind of tools that, in many cases, may considerably more than offset moderate variations in cost and may even make it worthwhile to make concessions in delivery, for

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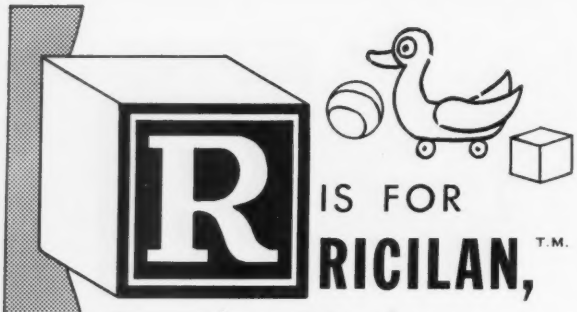

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instance: (1) assurance of uninterrupted production; (2) longer life and greater production from a particular set of tools; (3) avoiding the need for replacement of other parts of the press, such as cams and pressure rolls, that may become worn by poor quality tools; (4) better tablet appearance; and (5) elimination of break-in time (always more expensive than actual operating time) by having tools ready to run when received.

In contrast to the small job shop, the tool supply departments of tabletting machine manufacturers have a broad background of tabletting experience. They know their own machines better than anyone else does. They have a far greater stake in the success of the customer than does the small job shop, since not only are they seeking to protect their position with respect to the manufacture and sale of tools, but also they have a natural interest in providing tooling that shows up their machines in the most favorable light. These basic interests, coupled with their normal large volume of tooling business, puts them in a position to make sizable investments in personnel and facilities, which are far beyond the scope of the small job shop. These facilities represent a considerable tangible value to purchasers of punches and dies and can be summarized as follows:

(1) machine tools of the most modern type to assure highest quality at lowest manufacturing cost;

(2) the employment of metallurgists, researching in steels and heat-treating methods, to obtain tools that provide maximum life;

(3) laboratory facilities where tools are run with different materials to establish optimum operating conditions; and

(4) an engineering organization that devotes its exclusive time to tool design, an area in which new ideas are constantly being generated.

All of these facilities represent valuable assets which are at the service of the buyer of industrial tooling. When tools are purchased from sources having such facilities, tabletting departments have access to the most specialized skills available, not only for the solution of specific problems but, what is more important, for keeping abreast of new developments. Price, of course, remains an important factor.

In certain cases, expediency dictates the desirability of having tools manufactured in small job shops. However, if such sources are used to the exclusion of the machinery manufacturer, it may close the door to a useful combination of facilities that may be of considerable value to the tool user.

DIURETICS AND EDEMA

(Continued from page 467)

The inhibition of the action of carbonic anhydrase promotes diuresis by increasing sodium and potassium bicarbonate excretion in the urine and decreas-

ing excretion of ammonium ion. With this loss of bicarbonate the urine becomes alkaline, plasma bicarbonate falls, and a metabolic acidosis develops. Because of these properties, sulfanilamide began to be used as a diuretic agent in the management of congestive heart failure. Because of the unpleasant side effects of sulfanilamide, a search for less toxic but related substances was begun at Lederle. The most active of a series of heterocyclic sulfonamides was compound 6063, later called Diamox (2-acetylamino-1,3,4-thiadiazole-5-sulfonamide).

Diamox is rapidly absorbed from the gastrointestinal tract and almost completely excreted unchanged in the urine within 24 hours. Blood plasma levels are maintained for 6-12 hours after administration. The principle site of action of Diamox appears to be in the renal tubules where carbonic anhydrase is inhibited. Thus there is specific interference with the production of hydrogen and bicarbonate ions. The impeding of this acidification process which conserves base, results in a copious diuresis of bicarbonate, sodium and potassium ion, and water.

The continued daily administration of Diamox (a carbonic anhydrase inhibitor) is associated with a decreasing responsiveness, while the use of an oral mercurial diuretic is followed by a continued responsiveness in sodium excretion. Diamox causes a maximal excretion of sodium at a 250 to 500 mg. daily dose. Further increase in dose will cause no increased sodium excretion, but slight increase in potassium excretion. This is in contrast to an increasing dosage response seen with mercurial diuretics so that progressive increases in the dose of a mercurial diuretic is associated with an increasing diuresis. Diamox is best administered in a dose of 250 mg. every other day since tolerance develops so rapidly. This seriously limits its usefulness in all but mild cases of edema. However, the side effects have been very few. Cardrase (Upjohn) is very similar in action to Diamox, but on a weight basis is twice as potent.

Chlorothiazides

The search for more potent carbonic anhydrase inhibitors culminated in the synthesis of the most powerfully known oral diuretics, the chlorothiazides and hydrochlorothiazides. The introduction of chlorothiazide (Diuril; Merck S.&D.) was a most important advance in the treatment of edema because this was the first oral diuretic comparable in potency to parenterally administered mercurials. Diuril (6-chloro-7-sulfamyl-1,2,4, benzothiadiazine-1,1-dioxide) resulted from the observation that aromatic sulfonamides such as benzene 1,3-disulfonamide showed diuretic activity. If a chloro, amino or acylamino group is substituted on the benzene ring, the compound formed shows still higher activity, particularly with an acylamino group. Typical of these compounds is a 4-acylamino-6-chlorobenzene-1,3-disulfonamide. When this chemical is treated with alipha-

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tic and aromatic acyl diuretics, ring closure occurs between the sulfamyl group and the adjacent acylamino group to make a benzothiadiazine dioxide, most important of which was chlorothiazide.

Diuril was the first diuretic which avoided the salt retention drawback by inducing a large excretion of salt and water without risk of toxic effects or acidosis and without loss of effectiveness with continued use. Since sodium and chloride are excreted in nearly equal amounts, the acid-alkaline balance of the blood is not upset. Chlorothiazide acts like both a mercurial and a carbonic anhydrase inhibitor. *In vitro* it inhibits carbonic anhydrase, while *in vivo*, in larger doses, it acts like the mercurials by being a potent inhibitor of the renal resorption of sodium and chloride. Chlorothiazide may also promote the excretion of bicarbonate and potassium, due to its mild carbonic anhydrase inhibition. This increased loss of potassium with liability to potassium depletion makes intermittent treatment advisable, and often necessitates the concurrent administration of a potassium supplement. Chlorothiazide is rapidly absorbed on oral administration. Action begins within two hours and lasts 12 hours. This is in contrast to Diamox where the initial action occurs within six hours and lasts from 6 to 12 hours. Until the just introduced hydrochlorothiazide, the effectiveness of Diuril in producing diuresis was second only to that of the parenteral mercurials. While it is not as vigorous a diuretic as the parenteral mercurials it may be more effective in controlling congestive failure. The drug can be given over longer periods, thus preventing reaccumulation of fluid which may occur more rapidly than is advisable when using mercurials.

Recently hydrochlorothiazide has been introduced (Hydroduril of Merck S.D., Esidrex of Ciba, and Oretic of Abbott). This derivation of chlorothiazide differs from the parent compound in having the double bond in the heterocyclic ring saturated with two hydrogen atoms. Early clinical experience plus laboratory experiments showed that, weight for weight, hydrochlorothiazide was much more potent than chlorothiazide, but it remained to be shown whether this was a decided advantage. This is now definitely ascertained. The more than ten times potency of the hydrogenated derivative is not accompanied by increased side effects. The most significant difference between hydrochlorothiazide and chlorothiazide is concerned with potassium excretion. Potassium loss is considerably less with hydrochlorothiazide. The latter does not produce an increase in bicarbonate excretion and urinary *p*H such as occurs after chlorothiazide. The onset of action of hydrochlorothiazide is slower than the chloro analog (4-6 versus 2 hours), while the action lasts up to 24 hours in contrast to 12 hours. The diuretic effectiveness is maintained even on prolonged daily administration. In some instances hydrochlorothiazide may induce diuresis when mersalyl or chlorothiazide have failed.

The drug is particularly valuable in congestive heart failure, but claimed to be of lesser value in cirrhosis and renal disease.

The greater potency of hydrochlorothiazide may be related to better intestinal absorption. Unlike chlorothiazide, the dihydro derivative is not excreted in the bile and hence is more available for renal elimination and for greater action on the renal tubules. The renal clearance of both diuretics is more than the glomerular filtration rate, and the clearance of hydrochlorothiazide is greater than that of chlorothiazide. However, both drugs may cause electrolyte depletion in about 10 per cent of cases when dietary sodium is severely limited.

Ion Exchange Resins

A different approach to diuresis is by cation exchange resins which possess the properties of interfering with the absorption of sodium and potassium from the gastrointestinal tract. An example is Carbo-Resin (Lilly), which contains potassium to prevent the development of hypokalemia, or excess potassium loss. The most frequently used resins are the carboxylic cation exchangers. The usual dose administered to human subjects varies from 20 to 60 gms. a day. Patients find this medication objectionable, mainly due to the bulk. The added side reactions of nausea and vomiting have severely limited the use of resins in management of edema. They are reserved chiefly for certain refractory edematous states, such as Laennec's cirrhosis.

Steroids

A most recent addition to the clinical diuretic agents, but not yet commercially marketed, are the steroids that block the salt-retaining activity of aldosterone. The importance of aldosterone is that it is the most important secretory product of the adrenal cortex influencing electrolyte metabolism, particularly sodium retention. Apparently aldosterone acts by causing sodium to be reabsorbed and potassium to be excreted from kidney tubules. Since edematous individuals secrete high levels of aldosterone, Searle researchers worked on compounds with aldosterone blocking activity. Among the first and best compounds was SC-5233 or 3-3-oxo-17-β-hydroxy-4-androsten-17-α-yl) propionic acid γ -lactone, which blocked the urinary effects of aldosterone by reversing sodium retention and potassium loss. The mechanism of action appears to involve reversible competition by displacing or preventing aldosterone-like steroids from occupying key receptor sites in the kidney. Recently the acetylthio derivatives of the 17-spirolactones (SC-9420) has been demonstrated to possess about fifty times the oral potency of the previous compounds, enabling clinical studies at reasonable dose levels. The gamma lactone derivative of testosterone (SC-8109) has also demonstrated con-

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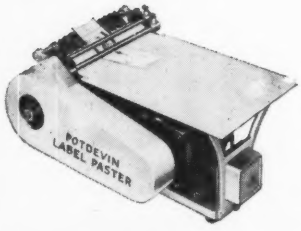

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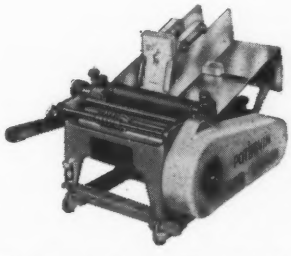

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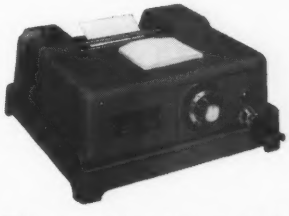

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siderable clinical promise, producing an increase in urinary sodium excretion, with a concurrent decrease in potassium. It is interesting that, after prolonged administration, a patient failed to respond to chlorothiazide, but diuresis was restored when chlorothiazide and SC-8109 were given together. Combinations of mercurials, chlorothiazides and steroids may be of value in producing diuresis in refractory patients.

Research Activity

Research continues at a high pace in the pharmaceutical laboratories of many companies. Squibb has announced Ademol, Bristol, Saluron (Flumethazide), with Hydroademol not far behind, with potencies and properties similar to chlorothiazides. The compounds differ from Diuril and Hydrodiuril only in the substitution of a trifluoromethyl group for the chlorine atom. Bristol Laboratories and the British Boots Pure Drug and Glaxo Laboratories are involved with similar trifluoromethyl substitutions of hydrochlorothiazide. Geigy has patented a large series of para-substituted benzenesulfonamides, with optimistic peroral diuretic claims. Available soon will be Daquin (Riker), a non-mercurial oral diuretic, developed in Europe. Daquin is a mild natruretic agent of the triazine chemical class. It is an effective diuretic without serious toxicity in oral doses of 300 to 600 mg. per day.

Electrolyte excretion patterns differ from those with mercurials, carbonic anhydrase inhibitors and chlorothiazide. The notable feature is greater effect on water than on sodium output. Daquin (N-para-chlorophenyl-2,4-diamino-s-triazine hydrochloride) is marketed in Europe as Ordipan. Its mechanism of action is not clear, but it is not a carbonic anhydrase inhibitor. Searle has also patented a series of aromatic substituted triazines. Potent diuretic activity is claimed for 2-amino-4-anilino-s-triazine. Practically the same compound was tested by Warner-Chilcott. Upjohn is conducting a clinical study of 10-[2-(1-pyrrolidinyl)ethyl] phenothiazine N,5-dioxide. Warner-Chilcott has tested Sulfocarbilate (p-sulfamyl-2-hydroxyethyl-carbanilate), a carbonic anhydrase inhibitor with relatively non-toxic properties. An extremely interesting group of sulfur-containing mercurials has been patented by Farbwerke Hoechst of Germany. The best is 1-(p-carboxybenzenesulfonamido) - 2 - β - propoxy) - 3 - (6 - carboxy - 2 - benzoxazolylthiomercuri) propane. Wyeth's Oraton is a xanthine mercurial (3-Hydroxymercuri-2-methoxy-1-succinimopropane theophylline hydrate. Lakeside has patented the mercuration products of 1-(2-pyrimidyl)-3-allyl urea. The same group at Lakeside has found that maleic acid has diuretic properties, which could be enhanced when the acid was administered in the form of certain diamine salts. A number of alkylene diamines were synthesized. Optimum diuretic properties were displayed by

N-(1-methyl-2-pyrrolidylmethyl)-N′,-N′-diethylenediamine dimaleate, indicating marked potentiation of activity. Sometime back Ciba was investigating a mercurial, diglucomethoxane, ['Mersroben'-3-(2-hydroxy - 3) - D - glyco - pentahydroxyhexo - mercap - tomercuri]-propyl-D-mannitol, but little has been heard of this sugar derivative.

Obviously, much work is going on, but most probably the agents of the future will be designed not only to relieve the edema, but also to help the underlying causative state of which the edema is only a symptom. This is already shown in the use of the chlorothiazides in hypertension.

ESSENTIAL OILS

(*Continued from page 461*)

"Sudden death" appears to be connected with the fungus *Valsa eugeniae*, the nature of which is not yet fully understood. It causes mature trees to wilt with little warning and to die within a few days; it attacks healthy trees in the prime of life and rapidly moves through plantations of trees 40 or more years old, leaving behind few survivors; curiously enough, these survivors are often those trees that were originally less vigorous. There is no known control for "sudden death." Experiments are in progress by scientists of the Department of Agriculture in Zanzibar with a view to halting the advance of the disease in the field by such means as trenching, liming, and the removal of the fungus from the branches of trees, where it is also found as an aerial "die-back" pathogen. The Department of Agriculture is also endeavoring to find the best way to rehabilitate clove plantations after they have been decimated by "sudden death." A feature of the disease is that young trees and saplings are difficult to inoculate with the fungus and are apparently resistant. For this reason young trees, planted in old "sudden death" areas, grow very well for perhaps 15 years and then slowly decline, their roots becoming infected by *Valsa*.

At the present time the Department of Agriculture is carrying out other experiments to insure that young trees planted in "sudden death" areas remain healthy. Probably resistance is connected with the general vigor of the tree, and possibly with soil conditions.

"Sudden death" in Zanzibar has reduced that island's contribution to the total exports of the Protectorate from one-third to about one-sixth of the whole, but production in Pemba is increasing, and has more than compensated for the reduced production in Zanzibar. Very large numbers of new trees are being planted every year and it is expected that the total production of the Protectorate will continue to rise.

As regards "die-back" disease, this is caused by the entry of the fungus *Cryptosporella eugeniae* into the tissues of the tree. Usually it is the result of

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careless picking and branch-breaking, and the consequent invasion of the wood by the fungus. The fungus may take years to travel down the branch, and older trees have many foci of infection. Eventually the death of the tree occurs after many years, when the fungus reaches the main trunk and succeeds in invading the whole cross-section of the wood. This disease of the clove tree can be prevented by avoiding branch-breaking when harvesting. In young trees the infection is easily cut out by pruning; the exposed surfaces must be protected by painting with a fungicidal paint. The young trees respond vigorously to this treatment, but it is probably uneconomic for older trees in which the disease has become much more prevalent. Widespread publicity on field management, combined with appropriate legislation, has in recent years had a most valuable effect in improving harvest methods.

It is impossible to assess the full extent of the damage caused by "die-back," but there is little doubt that clove crops would be at least 20 per cent greater if the disease could be checked.

The Clove Growers Association

A report on the clove industry of Zanzibar and Pemba would be incomplete without mentioning the Clove Growers Association, which since its formation in 1928 and its incorporation in 1934 has played such a predominant role in the Protectorate. It has helped the primary producers on the island by guaranteeing a floor price that assures a certain income to cover cost of production and allow a margin for living expenses. At the same time the Association protects users abroad against excessive price fluctuations by keeping large stocks in its warehouses—from which spice can be drawn in years of short crops. This policy has had a stabilizing effect on the local and overseas markets. The services rendered by the Association have greatly benefited the international clove trade as well as the agriculture of the Protectorate.

The Association purchases cloves from the growers, the quantity depending upon the size of the crop. In years of a bumper crop the Association may absorb the bulk of the crop, while in years of a short crop it may not purchase any cloves.

The Association disposes of its accumulated stocks by implementing the clove decree of 1938, whereby exporters are obliged to take a certain percentage of their shipments from the Association. At the present time an exporter must purchase 50 per cent of his shipments from the Association. The percentage may vary, however; it depends upon the size of the stocks held by the Association—the larger the stocks, the higher the percentage.

The prices at which the Association sells the spice to the exporters are established by the Board of Management, in accordance with the cost of production and overhead expenses, such as cost of storage and

handling, and shrinkage.

The Association also has the legal right to export cloves, but does not exercise it while the flow of exports continues normally; in other words the Association prefers not to interfere with private trade.

A grower is free to sell his crop on the open market in Zanzibar, and will probably do so if he is able to obtain a price higher than that offered by the Association. However, he cannot deliver an inferior product; the spice must meet the standards established by law, or will be refused when checked by the Produce Examiner of the Department of Agriculture. For example, cloves found to contain an excess of moisture must be dried again. Cloves purchased by the Association go through a second examination, this time by an official of the organization. All cloves must be checked again when brought to the export shed for export overseas.

There are many other activities which the law authorizes the Association to carry out; for example, it may act as land agent and auctioneer, as trustee and manager of agricultural properties; it may purchase agricultural implements for the producer, assist the grower by loans for agricultural development and for the harvesting of cloves, the latter being important to the growers at commencement of a new crop.

A major activity of the Association consists in the production of essential oil derived from clove stems. While the Association has an exclusive license for the distillation of both clove bud oil and clove stem oil in the Protectorate, it exercises at the present time only the right to produce clove stem oil—a product inferior to clove bud oil in both odor and flavor. (In the United States and in Europe the stem oil is used chiefly for the isolation of eugenol, the main component; and for the conversion of eugenol into isoeugenol, or vanillin.)

Export of clove stems from the Protectorate is prohibited, to prevent their use as an adulterant for clove buds. The stems are processed in the distillery of the Association, located near the warehouses in Malindi, and consisting of 12 large stills. Each still holds some 1,500 pounds of dried clove stems, or 2,000 pounds of clove buds. Steam pressure at the boiler amounts to about 80 pounds. Distillation of one batch of clove stems requires 16 hours, or 48 hours in the case of clove buds. The yield of clove stem oil averages 6 per cent, while that of clove bud oil varies between 15 and 17 per cent.

Still other activities of the Association are the export of copra, coconut oil, and coir fiber.

To summarize, the Clove Growers Association is a non-profit organization; it has no stockholders, and profits, if any, are spent on research, on the one hand, and on the other, for the general benefit of the agriculture of the Protectorate. •

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STOKES

(Continued from page 475)

den, but adds another cost in its place.

Capital invested in packaging material held in the pharmaceutical warehouse in preparation for immediate use when needed is just as real as capital burden for accounts receivable or for building expansion which may be required.

Procurement of frequent short runs results in voluntary captivation to limited sources of supply for greatest volume of stock items. Generally, a supplier must accept the short, unprofitable items if he wants the good volume items. This condition tends to reduce competition and may result in higher prices.

These problems are the direct result of packing prescription products in the traditional quantities simply because it is tradition. To eliminate these problems the following steps are recommended:

(1) Select the average (median) size tablet and capsule specialty.

(2) Select the ideal glass container for 100's, 250's, 500's and 1,000's of this product with minimum protective headspace and cotton cushioning.

(3) Design labels of appropriate sizes for these four packages.

(4) Select the closest approach to all-purpose closures and liners for the four packages.

(5) Design the indivdual cartons to hold these four fitted containers with pre-determined literature space allowance. (This step is not universally required.)

(6) Test pack quantities of each other size and shape capsule and tablet in these same containers at the same filling height as model (median) container. This will make cotton cushioning quantity also uniform.

(7) List quantities of each product to be packed in four sizes or less. When this is done, some products may not require a range of four quantities. The selling price of the final original package will determine its economic acceptability directly related to volume of the individual specialty and the ability of the retail pharmacy to pay.

(8) Invite the sales-production and purchasing management to confer with package development management.

(9) Recommend to the sales department that new price lists be prepared, the new lists to show cost to a pharmacy of the original packages and also cost per tablet or capsule in the original bulk stock package quantity.

In order to put this program into operation, new price lists are necessary. Otherwise, the pharmacist would have to handle a lot of mathematical calculations in order to arrive at a price for the customer. With the recommended price list, all the pharmacist

has to do is multiply the cost per tablet by the number of tablets.

The unit price of the product will speed prescription pricing and result in a reduction in the number of errors. Pricing of each tablet on the basis of the quantity cost will influence the pharmacist's pricing of the finished prescription. It should get the product to the consumer at the best price.

With this program of simplified package selection, future requirements can be based on aggregate usage experience rather than on a multiplicity of small estimates. Consequently one is in a position either to increase the quantities purchased at a time from one source, or to establish alternate sources, and the decline in demand of a once popular item or the failure of a new item to come up to expectations do not impose as great a risk in obsolescence of the container.

In general, the expenditure of the same amount of effort, time, and money on a considerably smaller variety of packages gives many members of an organization the advantages of concentration. Sixty minutes of attention concentrated on one problem often yields better results than ten minutes spent on each of six problems.

There are no rules requiring that a certain number of units be packed in each container. Only tradition stands in the way of streamlining the packaging end of the pharmaceutical dry prescription product business. •

(*Continued from page 459*)

U. S. PRODUCTION AND SALES OF SOME FERMENTATION PRODUCTS*

Fermentation Product	Year	Production, Lb.	Sales, Lb.	$ Value
Penicillin and salts	1956	631,000	593,000	63,529,000
	1957	694,000	601,000	66,299,000
Streptomycin	1956	130,000	147,000	5,604,000
	1957	198,000	169,000	6,786,000
Dihydrostreptomycin	1956	492,000	431,000	18,198,000
	1957	582,000	462,000	20,039,000
Neomycin and salts	1956	17,000	14,000	5,989,000
	1957	24,000	19,000	6,328,000
All others (broad spectrum excluding tetracycline	1956	477,000	366,000	105,148,000
	1957	465,000	430,000	113,627,000
Tetracycline	1956	220,000	186,000	72,903,000
	1957	404,000	299,000	108,466,000
Antibiotics for feed supplements, food preservation, crops	1956	779,000	683,000	28,108,000
	1957	870,000	795,000	31,307,000
Total antibiotics for human, animal and poultry	1956	1,967,000	1,737,000	271,371,000
	1957	2,373,000	1,986,000	323,596,000
Riboflavin for human, animal, and poultry use	1956	370,000	245,000	5,321,000
	1957	405,000	320,000	5,613,000
Vitamin B_{12}	1956	655	450	22,640,000
	1957	790	537	21,869,000
Hydrocortisone alcohol and acetate	1956	7,000	4,000	9,552,000
	1957	8,000	3,000	6,342,000

*U. S. Tariff Commission, Washington, D. C.

lelling sales increases for the most part, as general industry-wide domestic plant expansions are not in vogue. This may be partially influenced by production facilities installed in other countries, some of which are subsidiaries of U. S. firms.

Some unconventional applications of microorganisms are of interest. Microbial insecticides consisting of live spores of *Bacillus thuringiensis* are being tested against pests associated with alfalfa, corn, cab-

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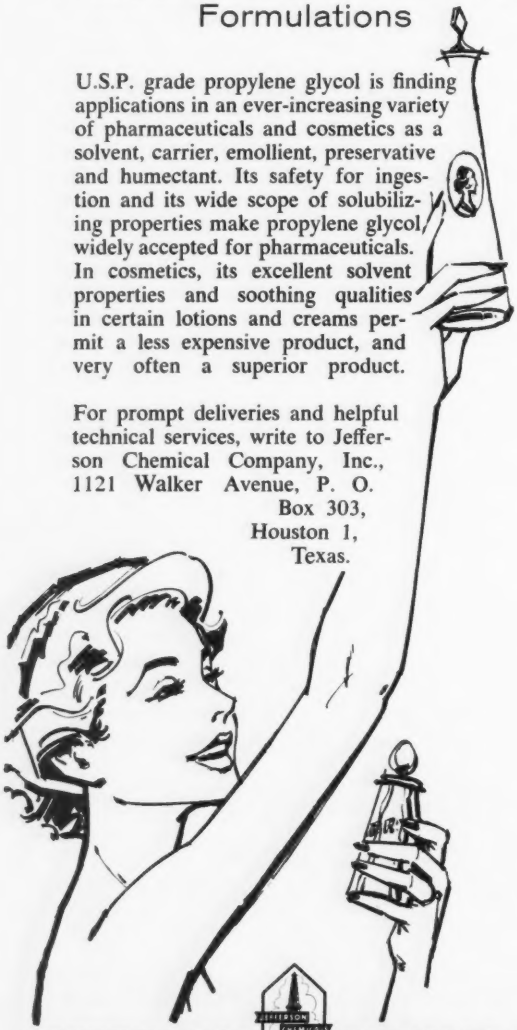

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bage, tobacco, and other crops. Soil flora which thrive on hydrocarbon gases may indicate petroleum deposits. Certain bacteria are being used to liberate oil from oil-bearing sands, sediments, shales, and tars. Bacterial acids leach copper, zinc, and iron and manganese from many types of low grade ores. Even "coal fermentations" are being studied as sources of new organic intermediates.

Microbes are being sought which can use noxious gases. Algae are being studied as oxygen, water, and food suppliers for future space travel. Bacteria are being exploited to remove grease from sewer lines and to destroy and detoxify phenol and formaldehyde waste liquors from chemical processes. It is hoped they may also destroy detergents in sewage treatment plants.

Plant Expansion and Production

The fermentation industry continues a world-wide expansion of operations. Domestically, expansions are small, except for research.

The U. S. Commerce Department recently announced that it will now allow export licenses of antibiotics and similar drugs to Russia and its European satellites. Included in the list are penicillin, streptomycin and dihydrostreptomycin, chlorotetracycline, oxytetracycline, and all similar antibiotics including sulfonamides. A total embargo is still in effect on Communist China, North Korea, and North Vietnam.

The general production figures on antibiotics production in Russia and its satellites are not known. A recent statement by Dremov of the Moscow Pharmaceutical Institute says that by 1960 antibiotic production will increase by 270 per cent over 1955. It is evident from this statement that present production is low as compared with U. S.

Amino Acids

Interest continues in the fermentative production of various amino acids. Merck & Co., Inc., has been licensed by Kyowa Chemical Co. (Japan) to produce L-glutamic acid by fermentation. Researchers at Kyowa also reported that the culture used in the L-glutamic process could be mutated to produce either L-lysine or L-ornithine. Merck is now in production with this lysine process.

Pfizer also continues to produce L-lysine by its fermentation process. The present price of L-lysine hydrochloride is now $4.95 per pound.

Vitamins

Considerable interst is still maintained in vitamin B_2 and B_{12} fermentations. A recent report shows that antimetabolites of vitamin B_{12} may be more effective in treating leukemia and other forms of cancer than the antifolic compounds now used. Recent tests involve use of the anilide and the ethyl amide of the monocarboxylic acid of vitamin B_{12}.

Antibiotics

Antibiotics remain the principal fermentation products and the mainstay of the pharmaceutical industry, particularly in the United States. The industry has grown rapidly in the United Kingdom, Western Europe, Eastern Europe, Middle East, and South Africa. Antibiotics account for more than 20 per cent of the monetary value of all pharmaceuticals produced in the United States.

Pridham and others have prepared useful classification of selected groups of *Streptomyces*, containing an excellent bibliography on antibiotics.

A concept of "lymphotropic antibiotics" was presented. Antibiotics and other crystalloid molecules circulate via the vascular system, with low levels in the lymph and lymph nodes. Macro-molecules have a particular affinity for the lymph system. Combinations of certain basic antibiotics such as streptomycin, neomycin, viomycin, and streptothricin with macromolecules such as sulfonic or phosphorylated polysaccharides were claimed to lower toxicity and blood levels but prolong blood levels and increase lymph levels.

Bile salts were reported to lower the minimum inhibitory concentrations (MIC) levels of neomycin for *Staphylococcus aureus* and penicillin for resistant strains but not for sensitive strains. For some other antibiotics, MIC levels were raised.

A conference on basic and clinical research on kanamycin was held in New York, July 1958. Waksman served as editor to present a summary of the practical applications of neomycin.

In spite of hundreds found in the past decade, several new antibiotics were reported during the year.

Antibiotic Chemistry. The chemistry of complex antibiotic structures continues to yield to the efforts of chemists. Particularly striking is the work of Patrick and others who have for the first time determined the structure of a polyene antifungal antibiotic, the tetraene pimaricin, which was shown to be a member of the macrolide family. Harman and others have reported the structure of another antifungal, eulicin ($C_{24}H_{52}O_7N_8$) which is not a polyene, but rather a complex amide. The isolation and structure of acetomycin ($C_{10}H_{14}O_5$) was also reported.

Amecetin B has been distinguished from amecetin. The former yields cytosamine on alkaline hydrolysis and *p*-aminobenzoylcytosine on mild acid hydrolysis. Amecetin also yields D-α-methylserine.

The structure of puromycin is 6-dimethylamino-9-[3-deoxy-3-(*p*-methoxy-L-phenylalanylamino)-β-D-ribofuranosyl]-β-purine. A structure has been proposed for the antibacterial macrolide, pikromycin. Blastmycin ($C_{26}H_{36}N_2O_9$), on alkaline hydrolysis, yields blastmycinone, 2-*n*-butyl-3-hydroxy-4-methyl-4-lactone, and blastmycic acid, *N*-(formyl-3-aminosalicylal)-L-threonine.

Chartreusin, ($C_{32}H_{34-36}O_{16}$), contains D-fucose, D-digitalose, and aglycone ($C_{19}H_{10-12}O_6$), which is a

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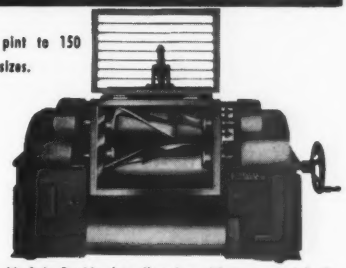

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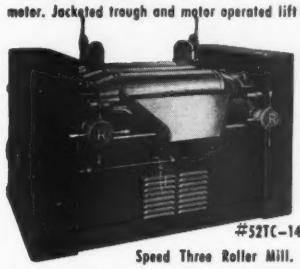

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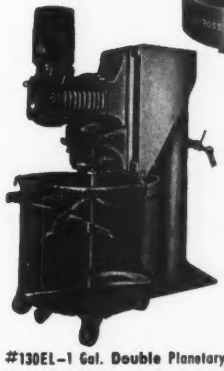

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derivative of *x*-methyl-2-phenyl naphthalene or *x*-methyl-2,3-benzofluorene containing a lactone group, two phenolic hydroxyls, and two oxygen atoms of unknown nature. One phenolic group is glycosidically linked to a disaccharide.

The pentaene fungichromin ($C_{35}H_{60}O_{13}$), on periodic oxidation, yields the chromophore 2-methyl-2,4,-6,8,10-dodecapentaenedial which is readily reduced to the diol with the same ultraviolet absorption as fungichromin. The alkaline degradation product of actidione is (+)*cis*-2,4-dimethylcyclohexanone. The polypeptide, polymyxin B, is thought to be an octa- or heptacyclopeptide with two or three amino acids on a side chain branched onto an α,γ-diaminobutyric acid end of the chain, joined to the carboxyl of isopelargonic acid. A new structural formula for gliotoxin is considered consistent with all chemical facts.

A six-membered carbocylic ring occurs in fumagillin. Dutcher has proposed a revised formula for aspergillic acid and hydroxy aspergillic acid.

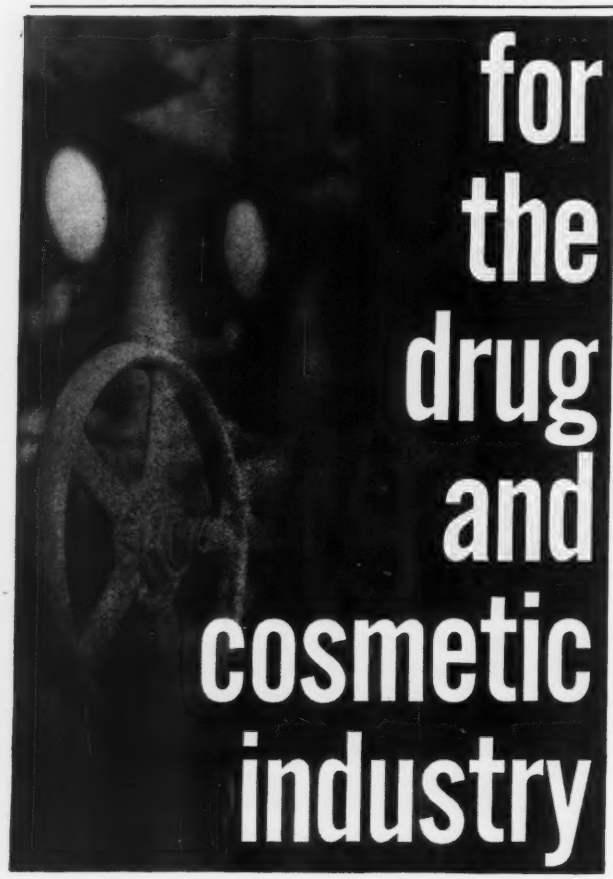
Trichoderma viride uses phenylalanine as a precursor to the indole moity of gliotoxin. Tryptophan and acetate were not used. The carboxyl of indole-2-carboxylic acid is the C_1 of phenylalanine.

The structure of kanamycin is essentially complete. Two hexosamine units occur, one of which is 6-deoxy-6-amino-D-glucose (6-glucosamine). Kanamycin B has been isolated by countercurrent distribution and Amberlite XE-64 chromatography. Hydrolysis of *N*-acetyl kanamycin B yields 2-deoxystreptamine and kanosamine; it does not contain 6-glucosamine. An unidentified ninhydrin-positive substance was encountered.

Tetracyclines. The past year has seen several new developments in the tetracycline series of antibiotics. Snell described a method for preparing radioactive oxytetracycline by using carbon-14 labeled acetate precursors. Boothe and others reported the total synthesis of a four-ring compound (± dedimethylamino-12*a*-deoxy-6-demethylanhydrochlorotetracycline) previously obtained as a degradation product from chlorotetracycline. The synthesis required some 30 steps.

By mutation of *Streptomyces aureofaciens*, the Lederle group has prepared other interesting analogs in this family. Active analogs, 6-demethylchlorotetracycline and 6-demethylbromotetracycline were obtained from the media containing the appropriate inorganic halides; 6-demethyltetracycline was prepared from both halotetracyclines by catalytic hydrogenation. The clinical effectiveness of 6-demethylchlorotetracycline was reported.

A biologically inactive analog of chlorotetracycline was found to be the product of another mutant of *S. aureofaciens*, 7-chloro-5a(11a)-dehydrotetracycline. On catalytic hydrogenation this substance was converted to tetracycline and a new isomer, 5*a*-epitetracycline, the latter being biologically inactive. Of



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further interest is the report that "normal" *S. aureofaciens* effectively hydrogenates 7-chloro-5a-dehydrotetracycline to the parent antibiotic, 7-chlorotetracycline.

Stephens and others, by hydrogenolysis of tetracycline under acid conditions with a palladium catalyst, obtained 6-deoxytetracycline among the products. Oxytetracycline yielded 6-deoxyoxytetracycline, and 6-demethyltetracycline yielded 6-deoxy-6-demethyltetracycline. This series of compounds does not undergo acid degradation to the respective anhydro products. The 6-deoxytetracycline and 6-deoxy-6-demethyltetracycline have been reported by others.

Two heptaene antifungal antibiotics were isolated from *S. aureofaciens*.

Shaposhnikov and others have reported a synthetic medium for the biosynthesis of oxytetracycline, containing starch, ammonium salts, and trace elements with yields of 1500 to 1900 μg./ml.

Doskocil and others studied the biochemistry of *S. rimosus* fermentations in relation to oxytetracycline production. Considerable pyruvic acid accumulates in the early phase (Gram-positive hyphae). Hyphae fragmentation follows, with pyruvic acid consumption. The fragments form secondary hyphae (Gram-negative) which produce the antibiotic and other pigments.

Tetracycline predominates in *S. aureoaciens* broths containing as little as 0.0025 per cent 2-mercaptobenzthiazole, particularly in the presence of bromide ion. McCormick and others have used 2,5-dimercapto-1,3,4-thiadiazole for the same purpose. Minieri and others employed deionized corn steep liquor.

Streptomycin. Workers at Takeda Pharmaceutical Industries have found a strain of *Streptomyces, S. humidis* n. sp., which produces dihydrostreptomycin as a direct fermentation product. This is a particularly interesting discovery. Another reduction product, dihydrodeoxystreptomycin can be prepared from streptomycin by an improved process if hydrogenation accurs in the presence of an amalgamated aluminum catalyst at *p*H 2.2. Dihydrodeoxystreptomycin is a clinically effective form of the antibiotic.

Penicillin. The biogenetic origin of the entire penicillin ring structure is known, with the exception of the thiazolidine nitrogen atom. The sulfur atom, carbon and hydrogen atoms of the β-lactone, and side-chain nitrogen atoms come from L-cysteine. The penicillamine moiety is synthesized from valine, but it is not known whether D- or L-valine is used. Nothing is known about the intermediates. Arnstein and Margareiter attempted to produce new penicillins using substituted cystines, without success. Derivatives of β,β-dimethyllanothionine and DL-penicillamine were not active as precursors.

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The biosynthesis and properties of 4-benzylphenoxymethyl penicillin were described. At *p*H 3 the new product was more stable than penicillin G or V, but blood levels were only about half those of penicillin V.

A particularly interesting finding was announced from the Beecham Research Laboratories in England. In the absence of acyl side-chain precursors (phenylacetic acid, etc.) *Penicillium chrysogenum* accumulates 6-aminopenicillanic acid, the nucleus of the antibiotic. This is consistent with the view that the acyl side-chain introduction occurs in the last stage of the biosynthesis. The nucleus compound has previously been encountered in small quantities in broths.

Although 6-aminopenicillanic acid itself is essentially without antibiotic activity, new penicillins are possible by using different acidic side chains. Perhaps another route to 6-aminopenicillanic acid is via side-chain cleavage from penicillin G.

NEW ANTIBIOTICS

Antibiotic	Producing organism	Properties
Aburamycin	*Streptomyces aburamiensis*	Acidic yellow crystals, m.p. 163°—5° C.; no N, S, halogen; solvent sol.; α_D+ 24.5 in methanol; UV 0.01N-NaOH234, 278, 316, 410 mμ. Orally tolerated; toxic I.P., IV; Gram positive; C, 55.57; H, 7.54; O, 36.89; similar to aureolic acid
Actinobolin	*Streptomyces*	$C_{13}H_{20}$—$_{22}N_2O_6$; Gram positive and negative; active vs. certain tumors
Albomycetin	*Streptomyces T-12-5650-115*	$C_{25}H_{44}NO_7$; α^{22}_D —48.7 (1% $CHCl_3$); gram positive; acidic; toxicity, mice, oral 1500 mg./kg.; IP 500 mg./kg.
Alomycin	*Streptomyces* sp.	Antifungal in broth and mycelium
Amaromycin	*S. flavochromogenes*	Active Gram-positive and Gram-negative coccii; not active vs. Gram-negative bacteria, molds, yeasts. C_{25}-$H_{39}O_7N$; m.p. 164.5° C. α^{25}_D + 6.2 (C 1%, ethanol)
Amidomycin	*Streptomyces*	Antifungal, solvent extracted. Degraded to D-valine and 3,6-diisopropyl-2,5-diketomorpholine. Inhibits: *Ustilago, Candida, Pyccinia, Hormiocium.* Not inhibited: *Oidium, Oospora, Aspergillus, Rhizopus*
Althiomycin		White crystalline; sol. dioxane, ethyl cellosolve, pyridine; insol. water, benzene; sl. sol. lower alcohols; decomp. 120°—160° C.; UV(0.03-NHCl)220—3, 285—90, 220—3, 235, 335 mμ; $C_{15}H_{14}N_4S_2O_6$
Cellocidin	*S. chibaensis* n. sp.	$(C_4H_4O_2N_2)_n$; absorbed on carbon, eluted with 80% methanol, concentrated, crystallized from hot aqueous methanol; m.p. 216° C. decomp. $E^{1\%}_{1cm}$ 290 at 299 mμ; active *tuberculosis* BCG 3 μg./ml. Structure: acetylene dicarboxamide
Croceomycin	*S. arabicus*	$C_{22}H_{18}O_6$; yellow needles; m.p. 325° C., decomp. α^{23}_D — 32 ± 4°; sublimes in vacuo 240 ± 260° C.; mg./kg. lethal for mice
Desertomycin	*S. flavogungini*	$C_{33}H_{60-62}O_{14}N$, m.p. 189°—190°; contains C-methyl, no N-methyl; active Gram-positive bacteria 1—25 μg./-ml.; very toxic, cytotoxic; coproduct of flavofungin
Duramycin	*S. cinnamomeus*	Polypeptide from antibiotic complex; active Gram-positive rods, some yeast and fungi; contains 9 amino acids, 2 with S
Enteromycin	*S. albireticuli*	$C_6H_8O_8N_2$; contains -COOH and -$COCH_3$; UV max. 300—320 mμ; α^{18}_D 0°; LD_{50} = 1.3 mg./10 gram mouse

Erythromycin A	*S. erythreus*	Separated from erythromycin B by recrystallization in nitromethane
Eurocydein	*S. abkilecticuli*	Antifungal; yellow, amorphous powder; UV 318, 332, 380 mμ; no S, halogen. LD_{50} = 0.22 mg./10 gram mouse IP
Fermicidin	*S. griseolus*	$C_{14}H_{2}O_4N_3$; α^{18}_D + 52.3; m.p. 96.8° C, LD_{50} = 180 mg./kg. mouse IV; 2 mg./kg. rat; active *vs.* yeasts and *Trichomonas vaginalis*, 0.05—0.2 mg./ml.
Flavofungin	*S. flavofungini*	Crystalline antifungal isolated from mycel-LD_{50} IP = 25 mg./kg.; nontoxic oral or SQ
Grasseriomycin	*S. griseolavendus*	Active *vs.* jundice virus; mol. wt. hydrochloride 610. Recovery via carbon absorption, alumina chromatography
Hygromycin B	*S. hydroscopicus*	Coproduct of hygromycin. Polyhydroxy base $C_{15}H_{28}N_2O_{9-10}$, one N-methyl, no O-methyl or C-methyl; Gram-positive and -negative activity, 6—100 γ/ml.
Hydroxymycin	*Streptomyces*	Similar to streptomycin and neomycin; differs by having pseudoneomine; low toxicity
Mitomycin C	*S. caespitosus*	$C_{54}H_{61}N_{13}O_{19}$; UV 216, 360, 560 mμ. Exhibits delayed toxicity
Mycobacillin	*Bacillus subtilis*	Mol. wt. 1800; 11.9% N, no S, halogen; ninhydrin-negative cyclic polypeptide. Acid hydrolysis yields aspartic acid, glutamine, serine, alanine, tyrosine, leucine, proline
Mycospocidin	*S. bobiliae*	$(C_{20}H_{32}[\ ]_2O_9)_n$; white crystal, decomp. 233—4° C. Active *vs.* spore former and acid-fast bacilli. LD_{50} = 1—2 mg./kg. IP
Nymbomycin		$C_{16}H_{14}N_2O_4$. Highly insoluble antiphage, *Streptomyces*, Gram-positive bacteria
Paromomycin	*S. rimosus forma paromomycinus*	$C_5H_{9-11}NO_2$
Phytoactia, phytostreptin	*Streptomyces*	Polypeptides; prepared for plant disease control
Pyoluteorin	*Pseudomonas aeruginosa*	$C_{11}H_7O_2NCl_2$; m.p. 174°—5° C., decomp. UV 255, 310 mμ; mol. wt. 268; structure given
Ramycin	*Mucor ramannianus*	Optically inactive, unsaturated hydroxy acid; m.p. 158°—160° C.; pK 4.6; mol. wt. 478; no UV
Raromycin	*Streptomyces*	Tumor inhibitory
Teruchiomycin	*S. eurodicus*	$C_{28}H_{43}NO_{10}$; needle crystals; m.p. 202°—4° C. decomp.
Toyokamycin	*S. toyokaensis*	$C_{12}H_{14}N_5O_4$; UV max. 230, 279, 339 mμ; LD_{100} IV = 20 mg./kg. Active *M. tuberculosis, Candida albicans*
Tubercidin	*Streptomyces*	$C_{11}H_{14}N_4O_4$; UV in 0.001 NHCl, 225, 270 *M. tuberculosis*
Virtosin	*S. olivochromogenous*	Colorless plates; m.p. 142.5° C., α^{18}_D + 80.5; $C_{27}H_{40}O_9N_2$; antifungal; LD_{50} IP = 0.8 mg./kg.
X-948	*Streptomyces sp.*	May be identical with echinomycin of Carboz; $C_{27}H_{40}O_9N_2S$, m.p. 237°—8° C.; α^{23}_D —308 in $CHCl_3$; Ba $(OH)_2$ reflex yields 2-quinoxaline carboxylic acid, NH_3
X-1008	*Streptomyces sp.*	$C_{29}H_{38}O_7N_6S$; m.p. 209°—16° C.; α^{27}_D —282°; $Ba(OH)_2$ reflex yields 2-quinoxaline carboxylic acid
Streptovitacin A and B		$C_{15}H_{23}NO_5$; isomeric compounds, used on experimental tumors
L.A. 7017	*Streptomyces sp.*	Gram-positive bacteria; yellow-green powder; UV 280, 430; acidic, α^{15}_D —155°, mol. wt. 1180; pK 5, 9.5
PA-128	*Streptomyces*	$C_{37-44}H_{61-75}O_{13-16}N_3$; UV 245, 285. Active *Endamoeba histolytica*, *T. vaginalis*; toxic orally
PA-147	*Streptomyces sp.*	3-Carboxy-2,4-pentadienal lactone

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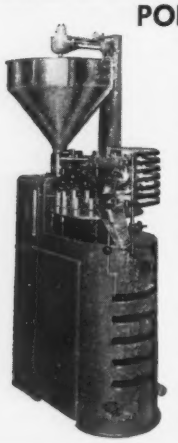

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thetic methods. These developments have probably caused a shift in production and marketing from the "wonder drugs" of only a few years ago to new candidates with improved pharmacological properties.

Of significance was a new chemical synthesis of aldosterone by a University of Wisconsin team. The Upjohn group began chemical testing of 6α-methyl-17α-acetoxyprogesterone (Provera) for the prevention of miscarriage and premature birth and as an oral contraceptive. It is claimed to be 300 times more potent than drugs now in use for this purpose.

The Merck group reported a new series of highly potent anti-inflammatory steroids, the 16α-methyl analogs of the cortisone family. Of these, 16α-methyl-9α-fluoro-Δ^1-hydrocortisone (dexamethasone, Decadron) is claimed to be the most active nonsalt retaining agent known. It was more potent than 16α-methyl derivatives of prednisolone, hydrocortisone, and 9α-fluorocortisone. Schering, too, entered the market with the same compound (Deronil) after announcing synthesis of the drug.

Until the 16α-methyl,9α-fluoro derivatives were introduced the older anti-inflammatory agents, cortisone, hydrocortisone, prednisolone, and prednisone, were in substantial competition with each other; 6-methylprednisolone (Upjohn, Medrol) and triamcinalone (16α - hydroxy,9α - fluoroprednisolone—Lederle, Aristocort; Squibb, Kenacort) intensified competition factors.

A simultaneous announcement from Merck and Schering teams introduced another new family of steroid, those with C_7 hydroxyls. The Schering group, by chemical means, prepared 7α-hydroxycortisone and 7α-hydroxyprednisone. The Merck biochemical syntheses resulted in 7α- and 7β-hydroxylations. The 7α-hydroxylations are accomplished by a *Helminthosporium* strain, with the 7β-hydroxy is introduced by a *Cladosporium* strain. Substrates successfully hydroxylated include progesterone, desoxycorticosterone, Reichstein's substance S, and cortisone.

Another simultaneous announcement by Upjohn and Syntex brought forth the 6α-fluoro steroid. The Upjohn report indicated that 6α,9α-difluoroprednisolone was 400 times more active than hydrocortisone as an anti-inflammatory, but salt retention was measurable. A powerful glucocorticoid (liver glycogen deposition activity) is 6α-fluorohydrocortisone, which does not cause salt retention; 6α-fluoroprednisolone, another potent anti-inflammatory, causes little or no salt retention. While the several fluorination reactions are accomplished chemically, useful hydroxylations required in the fluorosteroids are probably introduced by the several fermentation procedures of the industry.

The mechanism of biological hydroxylations remains of interest. The 7α-hydroxylation in the biosynthesis of cholic acid from cholesterol involves a direct replacement of the 7α-hydrogen. The same opinion is expressed for other hydroxylations. If deu-

terium is introduced into the 11β position, *Rhizopus nigricans* readily accomplishes an 11α-hydroxylation without affecting the marked 11β position.

Japanese workers have surveyed large numbers of fungi for steroid hydroxylations. Some 473 *Aspergilli* were screened for 11α-hydroxy- or 6β,11β-hydroxylations of progesterone. Only 21 out of 284 *Rhizopus* strains hydroxylated progesterone. *R. chinensis* gave a 50 per cent yield of 11α-hydroxyprogesterone. A *Syncephalastrum* sp. oxidized progesterone to dihydroxyprogesterone in two days.

Corynebacterium simplex can oxidize a 17-hydroxyl to 17-keto; 19-nortestosterone was converted to 19-nor-Δ^4-androstene-3,17-dione. Several *Mucorales —Mucor parasiticus*, *M. griseocyanus*, and *Helicostylum piriforme* oxygenated progesterone, deoxycorticosterone, 11-deoxycortisol, and testosterone to the corresponding 14α-hydroxylated products; 8β- (or 9α-) derivatives of deoxycorticosterone and of 11-deoxycortisol were encountered.

By strain selection, *Sarcina cerevisiae* can be propagated to contain as much as 11 per cent ergosterol.

PHARMACEUTICAL FUTURE

(*Continued from page 455*)

ready applied to cancer diagnosis and treatment will expand into broader areas of usefulness.

An anti-cold virus is close at hand with obvious health benefits, but with some fatalities for symptomatic products like nose drops, decongestants and paper tissues. Such tides of obsolescence is a built-in problem that the industry has learned to face, a small price for the tremendous progress that goes on. Change now comes so rapidly that all members of the health team shift readily to new products and techniques, leaving behind only a few die-hards that resist the new.

Our sights are on therapeutic agents that are safe, effective, and economical, because this industry can have no compromise with safety and efficacy and must use every possible faciiity for quality production, for automatic controls, for simplified organic and microbial synthesis to bring our products within the range of all people.

The pharmaceutical industry is spending $200,000,000 in research—roughly 10 per cent of sales—almost equivalent to profits, after taxes. Charlie Rabe pointed out that we waded through more than 100,000 compounds to bring through little more than 1½ per cent to clinical evaluation, less than half of 1 per cent reaching the shelves of the pharmacist. Even here, too many dreams dry up, and fail to survive the Voice's six-month check-up. Government, universities, and endowed research groups are planning to spend upwards of $600,000,000 to $700,000,000, of which NIH is earmarked for $400,000,000 so that the American public has behind it close to a billion dollars of research in the health field.

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The program is so vast that even today electronic data processing equipment is used to systemize and maintain the accumulating facts, and minimize hours of backtracking and duplication of research efforts. Electronic brains will store, retain and deliver on request the precise scientific data we need.

With this tremendous program at work with an industry willing and able to back research with other millions in manufacturing facilities, pharmacy must expect large increases in prescription and accessory sales, estimated to increase at least 50 per cent by 1965. The pharmacist is the primary distributor, whether in a retail pharmacy or hospital. His essentialness is assured by the multiplication of medicinal formulas not available today. Their complexity, their precision characteristics, and the trend toward increased potencies place the pharmacist in the key role of advisor to the physician, and guardian of the public health.

The demand for trained men and women is constantly growing. Considering the expanding field and the certain advance in population, the pharmacist has little time to perfect his talents for emulsions or suppositories. His great service to medicine will be measured by his knowledge, his expert judgment, and his close coordination with the physician's plan, and with dependable dispensing. His prescription will be compounded more with priceless know-how than art and manual skill.

In the area of the administration of health services there will be progressive, evolutionary change in training, education, prepaid health programs, and in distribution. Education particularly needs strong faculties, and that is the prime interest of the American Foundation for Pharmaceutical Education, which needs far greater support than it is now receiving. Another great need is well trained pharmacologists. We see increasing centralization of health services, in the military area, including dependent civilians, in medical centers, and in group health programs, some of which are organized by labor groups, civil service groups, and community groups.

The industry lives to a large extent under the discipline of certain regulations. These will grow in scope and severity. There is excellent discipline within the industry, a reflection of the medical conscience. The industry has undertaken to do its part in observing a right conscience about its business and practices. Through better horizontal association and more active coordination, as we are doing this week, there

will be a broader appreciation of the interests of all segments of our industry; and, particularly, mutual confidence in the work each of us is trying to do.

Where self-regulation fails to do its job, you can be certain regulation of one kind or another will move in as a corrective. Like most Americans we treasure freedom of thought and action. We are confident we can progress faster and better through our built-in incentives, but, when the public interest requires traffic lights or guide lines, this industry will adjust itself to reasonable essential regulation, especially if the interest of the patient is better served.

There is a certain type of publicist or politician who feels the excitment of popular interest in the prices of drugs. You know that confusion reigns because the prices of today's potent drugs are compared with popular prescriptions for symptomatic concoctions of two or three decades ago. And yet, the prices of individual drugs have frequently gone down, never up. In per cent of spendable income we see an up in 1958 at 1.03 per cent of disposable personal income, but in 1957 it was 0.95 per cent versus 0.98 per cent in 1956, and 0.94 per cent in 1933. But look what the physician has to work with now, and consider the miracles accomplished by today's medicine!

PHARMACEUTICAL RESEARCH

(Continued from page 463)

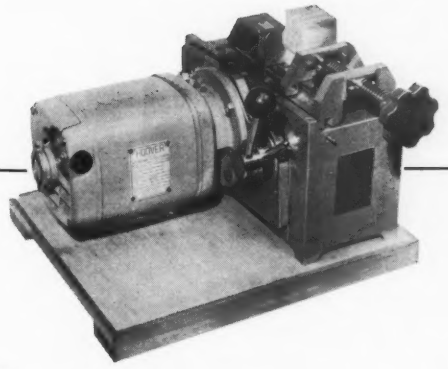
the companies launched mass screening programs. The Sprague-Beyer team, which consisted of people from several different scientific disciplines, chose a more selective approach. They felt they had accumulated enough theory, knowledge, and experience under the renal program to go directly after exactly what they wanted.

What they wanted was a drug that would excrete sodium and chloride—or table salt—not sodium and bicarbonate. Current doctrine about the kidney held that this objective was unattainable. But the Beyer-Sprague team had developed its own doctrines and finally produced a drug, Dirnate, that would do what others said was impossible.

The excitement mounted as the pharmacologists announced that the animal tests showed that Dirnate was an effective oral diuretic. The pathologists and toxicologists pronounced it safe enough for evaluation in human beings.

When the first clinical reports came in, the team working on the renal program was in for a shock. Despite all the early optimism, Dirnate had turned out to be medical failure number three. Too many people could not absorb it into the blood stream when it was administered in tablet form. Despite its medical failure, however, the new drug turned out to be a scientific success. It demonstrated that a saluretic agent such as they envisioned could be produced.

A saluretic agent, that is, one that will cause the



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excretion of salt, attracted Beyer and Sprague for a special reason. If they could get a satisfactory agent of this sort, they just might hit upon a drug that would be a great boon to sufferers from hypertension, many of whom were sentenced to a tasteless low-salt diet to keep their blood pressure down. Increasing the elimination of salt should have the same effect as not eating it in the first place, they reasoned. Seven years later, they had the satisfaction of finding out that their reasoning was sounder than their fondest dreams.

When the renal program reached its tenth anniversary in the middle of 1953, it ran into heavy weather. Nothing that would help pay for the cost of such a long-range basic project had developed from it, except Benemid. Dr. Beyer's description of the ideal drug he was looking for had been denounced as visionary. When his paper on this subject was published in a scientific journal, the decision was about to be reached that it would be best to call it a day and go in search of more hopeful prospects.

Into the middle of this dilemma, a Merck Sharp & Dohme competitor—Lederle—dropped a bombshell, a new diuretic called acetazolamide or Diamox. It was such an immediate medical and commercial success that it made two things apparent. First, it showed the eagerness of physicians for an improved diuretic, and, second, it showed that continuation of the renal program would be a lot better financial gamble than anyone had previously thought.

This, of course, is exactly the kind of situation to which the pharmaceutical industry is organized to react. In essence, we are a sensitive mechanism for translating the needs of physicians into new research projects. The hope of the profit we might reap, if our laboratory is successful in finding the needed product, is enough to justify the risk that we might fail, as we do again and again and again.

The new turn of events had turned the renal program into just such a risk, and it was not only continued, its pace was accelerated. Dr. Sprague put four groups of chemists on the job of synthesizing new compounds, hoping one of them would crack the problem. A young chemist named Dr. Frederick C. Novello was put in charge of the group that was given the aromatic sulfonamides, one of the least promising territories.

Dr. Novello's group worked, ate, and slept aromatic sulfonamide chemistry for six intensive months until, in October 1954, they were encouraged by finding a sulfonamide which produced a high order of sodium excretion. Then in May 1955 came a real breakthrough: synthesis of the first compound of the chlorothiazide class. It showed a high order of chloride as well as sodium excretion. Dr. Novello's reaction to this change is worth hearing in his own words:

"Working in this field," he said later, "is extremely exciting to the chemist. Most areas of organic chem-

istry are pretty well worked over but here was a very obscure one. This was a class of chemistry that was all ours. We had a nice secret all to ourselves. It was a chemist's dream come true."

The other three groups were shifted to this new type of chemical. Getting closer to their goal with each new compound they synthesized, they finally reached it five months later when they hit chlorothiazide itself, which excreted sodium and chloride in almost equal amounts. We gave it the trade name Diuril. The patent has Dr. Novello's name on it.

Synthesizing Diuril was, of course, only the first step. Before it could be clinically tested on human beings, it had to be exhaustively proved on animals. This was the province of Dr. John E. Baer, the pharmacologist who had already been working with the renal program for four years. He had charge of a team of pharmacologists, pharmacological chemists, physiologists, pathologists, enzymologists, and toxicologists who had been working as closely together as had Beyer and Sprague.

Large numbers of mice, rats, and dogs were chosen for the experiments. The dogs were examined for blood and urine chemistry and hemoglobin and were given complete physical work-ups, including electrocardiograms, several times before being put on Diuril. This was done in order to establish absolute norms. Then they were given enormous doses of the new drug—sixty times those that would later be prescribed for humans. None died. None was even sick.

Every day for months they were kept on massive Diuril therapy and Dr. Baer's group periodically checked hundreds of physical factors, looking for changes. The drug was traced through the body to make sure that it had no long-range deleterious effects and that it was not accumulating anywhere. Finally, exactly one painstaking year after its synthesis, the pharmacologists announced that Diuril was ready for clinical testing on man. In animals it was not only effective; it was quite safe.

Diuril was then unveiled for a select group of seven kidney physiolgists—two of whom were from the National Heart Institute—at a day-long meeting in October 1956. They were asked whether they would like the new drug for clinical testing. Their response was so favorable that not enough Diuril was available to satisfy their demands.

Then began the careful, painstaking clinical testing on as wide a scale as possible, which this company always requires before putting a drug on the market. The clinical testing went on for 14 months, giving the medical profession ample time to learn from the best investigators all about the drug's strengths and weaknesses before it was released for prescription use. By June 1957, Dr. Augustus Gibson, our medical director, had distributed it to 250 selected clinicians in the United States and 54 physicians in 18 foreign countries. It went to physicians in every teaching hospital in the nation. The specialties of

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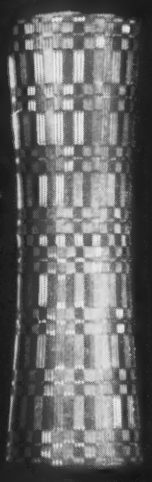

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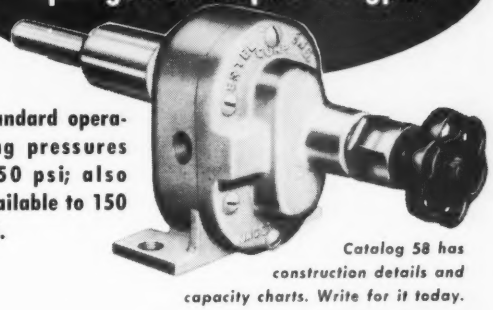

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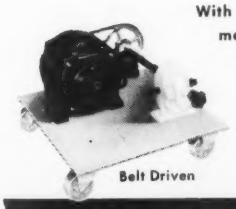

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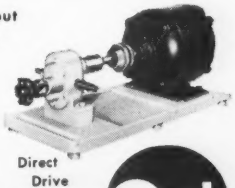

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these investigators included internal medicine, gastroenterology, obstetrics and gynecology, endocrinology, cardiology, pharmacology, ophthalmology, and pediatrics. As Dr. James Watt, Director of the National Heart Institute, has pointed out elsewhere, several of these men were already working in the cardiovascular field under grants from the National Institutes of Health. By the time we released Diuril to the medical profession, following its careful consideration and subsequent release by the U. S. Food & Drug Administration, over 1,000 physicians had tested it on patients.

Even though Diuril had come all the way from its first synthesis to clinical trials, it still had some distance to go before it could be administered to patients. It had to be manufactured on a large scale. Whole new sets of disciplines then came into play—from financial planners to chemical engineers.

The process had to be worked out and constantly improved. Pharmacists, chemists, and others had to work out usable dosage forms—an exciting and difficult assignment in trying to forecast the forms of a new drug the practicing physician will decide are most convenient and effective for him and his patient. Sales had to be forecast and then upped almost weekly as the encouraging results of the clinical investigation began to come in. A new plant had to be built at the cost of more than $1.5 million. Distribution and marketing plans had to be developed. And, toughest of all, the production people had to face rapidly mounting estimates of the targets they had to meet. In the end they had to raise output from a 300-kilograms-a-month pilot plant to facilities for turning out 650,000 kilograms a year. In addition, we went forward as quickly as possible with plans for producing the drug in several foreign countries.

Part of the anatomy of pharmaceutical industry research involves all doctors. I am not speaking of doctors as clinical investigators, but as practising physicians. The rate at which we are able to contribute to the improvement of the health of the American people with new and effective remedies is dependent in large measure on how fast we can get them from the stage of clinical testing to the patients who need them. It is one thing to make a great discovery in a laboratory. It is quite a different thing to translate that discovery into the actual relief of pain and suffering for several hundred thousand men, women, and children scattered across the land.

Our research, production, and distribution teams did their best. They found the drug, synthesized it, tested it, produced it against a frightful schedule, and had enough ready so that it could be prescribed the day it was released in January 1958. In the meantime, Merck Sharp & Dohme had done its conservative best to tell doctors what was coming. It was now up to them to evaluate the clinical reports and decide whether Diuril would stay on the drugstore shelves, or whether they would give it to their patients.

Before the first month was out, half the patients in the country on diuretic therapy were getting Diuril. Its use in the treatment of hypertension—bettering the prediction Dr. Beyer had made even before the drug was born—has also been quite impressive. About 50 per cent of the Diuril prescriptions now written are for that purpose. We estimate that today in the United States alone, more than one million diuretic patients and about 500,000 with hypertension are benefiting from this drug.

With the discovery, production, and use of Diuril, the renal program, now in its 17th year, has by no means come to the end of its journey. The release in January of this year of HydroDiuril, a more potent chlorothiazide analogue, is an indication, I hope, of good things yet to come.

The repercussions of the renal program, however, are not confined to Merck Sharp & Dohme. The competitive energies of the industry have been aroused. The success of Diuril has set off one of the most exciting races in molecule manipulation in recent times.

Patents protect our past research and thus enable us to recoup our costs when we hit a new and effective remedy. But they are not an iron-clad protection against the future. As a matter of fact, even before the issuance of the Diuril patent, two scientific papers disclosed its exact chemical structure to our competitors, and the molecule manipulation began even before we could put our product on the market.

The results are already beginning to pour in. Ciba came out with hydrochlorothiazide almost at the same time we did. The past few months have seen a growing tide of announcements about new compounds, all of which have a structural relationship to Diuril. To date, such announcements have already come from the laboratories of Squibb, Schering, Bristol-Myers, and Pfizer. And Abbott has become the third company to market hydrochlorothiazide. The patent lawyers are pretty busy these days. Theirs is an important discipline in a pharmaceutical company, for any industry that depends as much as we do on research needs patent protection for its past discoveries in order to be able to finance its future contributions to the growth of medical knowledge.

Though the final returns to medicine from the renal program will not be known for many years to come, this is as good a time as any to look back and try to understand what we have learned. We could pick out many things on which to focus our attention. I should like to mention just two.

The first is the constant interaction—running all the way through the years—between fundamental and applied research, each one feeding on, and, in turn, nourishing the other. This is the result of what I believe to be one of the great achievements of the pharmaceutical industry, the happy marriage between two strong human incentives: the quest for new knowledge, on the one hand, and the pursuit of financial success, on the other. This speaks well, I

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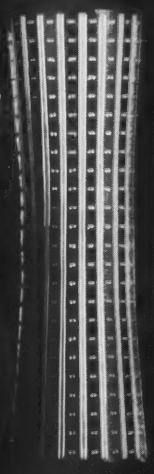

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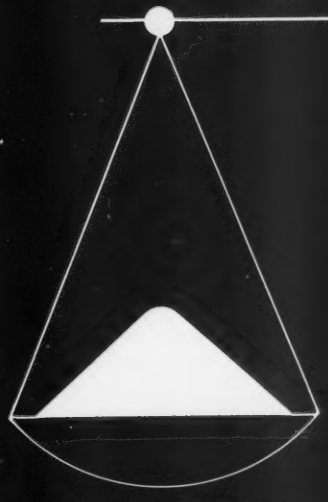

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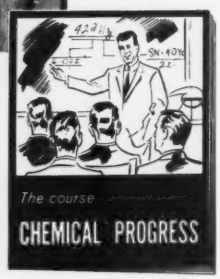

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think, for the future of our society, so dependent as it is on the cooperation of industry and science.

Finally, I would like to focus our attention on something that is perhaps even more important. That is the way so many diverse disciplines, loyalties, and objectives, represented by a vast number of people, worked together under considerable pressure and at impressive speed to produce a beneficial result.

Within Merck alone, men and women trained in some 50 professional specialties, from mathematics to pharmacology to chemical engineering, have developed a kind of teamwork that is not found today on a university campus. In fact you would be hard put to find its equal in peacetime anywhere except in an industrial company.

But our people would hardly have gotten anywhere had it not been for the organized and at the same time voluntary cooperation of countless outside individuals and groups—from the pioneers of scientific thought to the pharmacist who owns a corner drugstore in Iowa.

PACKAGING: AN APPLIED ART

(*Continued from page 479*)

will be packaged. He may use commonplace materials in designs of crude vigor, or he may use beautiful materials, refined detail, and perfect execution in designs of extraordinary elegance. In either case the aesthetic quality of the package, as of other artifacts, is the result of a conscious effort to organize materials and functions into clear shapes and relationships, with a due concern for their effect on the eye."

Among the other re-usable packages shown were a molded polyethylene tank with spigot, and a polyethylene drum with pouring spout by the Delaware Barrel and Drum Company, Inc.; a polystyrene Surgiset (1954), designed by Lippincott & Margulies, Inc., for Ethicon, Inc.; a plastic bottle by Modern Decorating; a Polyvial with captive cap, by Olympics Plastics Company, Inc.; and a polyethylene dropping container designed by E. C. van Schiak for Vaessen-Schoemaker Holding, N. V., Holland.

Among the disposable packages shown were Chanel's company-designed box for Chanel No. 5 powder and cellophane wrapping and paper seal for soap, (both 1924); a collapsible metal tube from the Collapsible Tube Manufacturers Council; a folding accordion carton, and Kliklok, cardboard protective packaging, from the Container Corporation of America; a rigid aluminum container, Continental Can Company; another rigid aluminum container by Ecko-Alcoa Containers; a cologne box and the large glass bottle for Aphrodesia eau de cologne, both company designs of Faberge, Inc.; Drumpaket, by the Gaylord Container Division, Crown Zellerbach Corporation; the box for Preludin, J. R. Geigy S.A..

Switzerland; Ro-Con fibre drum by Greif Bros. Cooperage Corporation; a rigid plastic dispenser for Band-Aid adhesive tape, by Johnson & Johnson; an aluminum can by Kaiser Aluminum and Chemical Sales, Inc.; Dylite, expandable polystyrene package, designed by Lone Star Plastics Company, Inc., for Koppers Company, Inc.; the cardboard box for Wash Up!, designed by Brownjohn, Chermayeff & Geismar for Lensclean, Inc.; a milk-glass bottle for mouthwash designed in 1879 by the Odol Chemical Corporation; Vert et Blanc Flowers, designed by Charlotte de Peillon for Parfums Carven; a styrene mold holder for medical syringes and vials, by Plaxall, Inc.; Aero Meter nasal spray, by Rexall Drug Company; rigid aluminum containers by the Reynolds Metals Company; Triaminic tablet dispenser, a company design by Smith-Dorsey Pharmaceuticals; molded urethane foam packaging, Stanfoam, by Standard Plastics, Inc., for Machlett Laboratories; both foil-laminated and vinyl Ultrapak for liquids, by William Stevens Company; bottle sleeves of folded paper designed by the Industrial Design Department, University of Illinois; and a glass bottle for serum by the T. C. Wheaton Company .

COSMETIC EMULSIONS

(*Continued from page 465*)

range. Soaps, added as such or prepared *in situ*, have the weight of tradition behind them and permit the easy formulation of good emulsions. Since soap emulsions are sensitive to *p*H, however, and to many chemicals, they may be somewhat circumscribed as effective vehicles. Numerous cosmetics based upon soap formulations could be improved by reformulation on a non-soap basis. A properly selected synthetic anionic emulsified does not share the limitations of soap and will produce stable, cosmetically attractive emulsions. A direct exchange of a synthetic anionic emulsifier for a soap in a formula, however, will not usually lead to an emulsion with the same physical properties.

Larger proportions of nonionic agents, when used as primary emulsifiers, must be used in comparison with ionic emulsifiers, but the resulting preparation will be stable and effective with a large number of additives and over a wide *p*H range.

Cationic emulsifiers, making very good emulsions, are often selected because of additional inherent properties, such as antibacterial action and substantivity to the skin. They are often useful only in acidic products and have greater reactivity than nonionic emulsifiers.

Choice of the type of emulsifier, and of the specific one being considered, should be made with full awareness of the chemistry of the emulsifier and of the other components of the mixture. An emulsifier

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may be inactivated by slow hydrolysis in the *p*H range preferred for the emulsion; it may form an insoluble compound without surface active properties with other emulsifiers in the system, or with other components. Although not emphasized in this discussion, the physiological properties of the emulsifier (as well as of other ingredients of the mixture), such as toxicity, sensitizing potential, irritating power, promotion or retardation of absorption by the skin, must be well understood in advance.

Finally, preparation of the emulsion warrants a number of comments. By the use of larger quantities of the emulsifier combination, an emulsion may be prepared with a minimum of mechanical energy, or with really inefficient agitation. Such a product may be satisfactory; but it will not be as good as it could be. Heat and mixing should not be limited to the directions "65° to 75° C. and stir until homogeneous." A specific temperature may be required for maximum "hydration" of the auxiliary emulsifier and reproducible viscosity; the effective action of an homogenizer may give a finer particle emulsion of greater stability with far less emulsifier. Even the traditional two-kettle means of making emulsions may in many instances be altered by adding all ingredients to a single tank, followed by melting, minimum agitation and homogenizing. An emulsion should be a system at equilibrium, and changes over a period of time indicate that equilibrium has not been attained in the manufacturing process. Selection of preparative conditions, with special emphasis on temperature and subdivision, should in most instances result in products that undergo little or no physical change with time.

SCC SEMINAR 1959

(Continued from page 536)

were determined at timed intervals. The effects of area, concentration, vehicle, and substituents were studied by *Dr. V. Cotty* of Bristol-Myers Company.

Topical application alone or as a supplement to oral therapy has been used extensively with excellent results in the case of vitamin A and panthenol, according to *Dr. Saul Rubin* of Hoffmann-La Roche, Inc. Panthenol shows excellent healing properties when applied to burns, wounds, ulcerations and other lesions of the skin and has been particularly successful in older individuals with circulatory disturbances where normal epithelization does not progress satisfactorily. It has also been used widely as an ingredient of hair preparations.

The widespread and continuous use of cosmetics makes it imperative to develop information not only regarding the beneficial physiological effects of their components but also regarding their potential unfavorable actions on the skin as well as systemic reactions. A variety of possible cutaneous effects and examples of procedures which may be utilized effec-

tively for each, were presented by *Dr. Raymond R. Suskind* of the University of Cincinnati. These include (1) primary irritation, (2) allergic sensitization, (3) photosensitization, (4) interference with pigment formation, and (5) damage to specific cutaneous structures including the appendages. There are definite limitations to standard procedures of appraisal.

Multiple exposures of nickel sulfate in the presence of sodium lauryl sulfate cause skin irritation in guinea pigs. Either agent alone has no effect. *Dr. L. J. Vinson* of Lever Bros. used this system for the purpose of studying the influence of different surface active agents on percutaneous absorption.

Results show differences that exist between anionic surface active agents in eliciting the $NiSO_4$ skin response in guinea pigs. $NiSO_4$ (0.5%) penetrates the dermal layer in the presence of one per cent sodium lauryl sulfate or sodium dodecyl benzene sulfonate with allergenic contact dermatitis ensuing. In the presence of soap, one percent sodium acyl isethionate, or acyl methyl taurate no skin response to $NiSO_4$ is observed. Also negative findings were obtained when guinea pig skin was treated with $NiSO_4$ in the presence of nonionics and a cationic.

Systemic toxicity resulting from the absorption of cosmetics applied to the skin is not a major problem for the industry. It is, however, an aspect of the safety evaluation program that cannot be ignored.

For a material to exhibit the property of percutaneous toxicity, it must (1) penetrate the skin sufficiently to reach the general circulation, and (2) be inherently toxic toward the organism.

Various approaches to the investigation of percutaneous toxicity were discussed by *Dr. Fred H. Snyder* of Procter and Gamble, using as examples both cosmetic materials and other compounds that have frequently been used in products applied to the skin.

The various categories of cosmetics and the reactions produced were illustrated by *Dr. A. Rostenberg* of the University of Illinois. Theory of the mechanisms by which the reactions are brought about was discussed and the precise chemical in the cosmetic responsible for the reaction was considered where this was known.

Hair dyes, hair wavers, hair straighteners, lipsticks, anti-perspirants, nail polishes, and perfumes were considered. The reactions from hair dyes are those of toxcity plus those of eczematous sensitization. Hair wavers and hair straighteners produce reactions primarily on a primary irritant basis.

Cheilitis from lipsticks was discussed, and folliculitis and deodorant granulomas as reactions to anti-perspirants.

Eczematous sensitization reactions to nail polishes and accessory nail cosmetics were considered, and photosensitization or the development of a dermatitis as a manifestation from perfume. •

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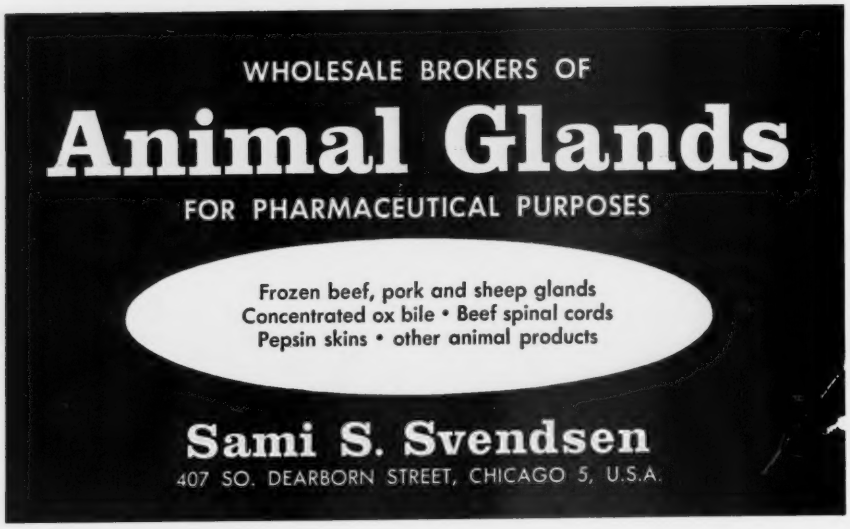
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